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TYPHUS FEVER
WITH PARTICULAR REFERENCE TO THE SERBIAN EPIDEMIC

BY

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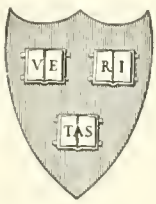

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TYPHUS FEVER
WITH PARTICULAR REFERENCE TO THE SERBIAN EPIDEMIC

PART I

TYPHUS FEVER WITH PARTICULAR REFERENCE TO THE SERBIAN EPIDEMIC

By RICHARD P. STRONG

The epidemic of typhus which occurred in Serbia in 1915 was one of the most severe which the world has known in modern times. It not only interrupted and suspended for approximately six months all important military activities of the Serbian army, but it also delayed the military advance of the central powers against that country during this period. The epidemic was moreover particularly characterized not only by its magnitude, but by its high virulence and high mortality. During the height of the epidemic the number of new fever cases entering the military hospitals alone reached as high as 2500 per day, and the number of reported cases among the civilian population was approximately three times this number. How many more unreported cases actually occurred, one will never know. The mortality during the epidemic varied at different periods in different localities between 30 and 60 per cent, and in complicated cases sometimes reached 70 per cent. Over 150,000 deaths occurred within six months before the epidemic could be suppressed. Coincident with the epidemic of typhus there occurred an epidemic of relapsing fever, and there was present much typhoid fever. Under the conditions existing at the time in Serbia, often little discrimination in the diagnosis of the nature of the fever could be made, and most cases of fever occurring in the army were sent or found their way to the military hospitals which were practically all used for typhus cases during one period of the epidemic. These individuals, if they actually did not have typhus on entering a hospital, were, in the early stages of the epidemic at least, very liable to contract the disease. The figures of fever cases which I have given therefore

include the cases of relapsing fever and of mixed infection with typhus and this disease, as well as a number of cases of typhoid. It has not been practicable for the writer, particularly on account of almost continuous foreign service during and in connection with the war, to publish before an extended account of the activities of the American Red Cross in connection with the suppression of the typhus epidemic in Serbia. Even today much statistical material collected in Serbia in connection with the epidemic is not at hand for inclusion in the report. However, on account of the very wide prevalence at the present time of typhus fever in epidemic form in Eastern and Central Europe, and of many problems to be met in relation to the eradication of these epidemics, it has been considered advisable to summarize the Serbian experience and to publish without further delay the report in its present form.

Conditions in Serbia Relating to the Epidemic

It will be recalled that before Serbia had time to recuperate from the Turkish and Bulgarian wars of 1912 and 1913, she was plunged into the third and greatest world war in 1914, which obviously taxed to the utmost all her resources. The previous wars she had undergone, accompanied by outbreaks of disease, notably of cholera in 1913, had already considerably reduced her available medical personnel and her hospital and sanitary supplies. Serbia thus war-worn and weakened, with her resources already greatly overburdened, was in no position to combat such an epidemic as that with which she was confronted in 1915, and when this outbreak of disease was well started it spread almost unrestrictedly throughout the land. There were only approximately 350 Serbian doctors in the country prior to the outbreak, and these bravely took up the fight against typhus in 1915, but their number grew less day by day, and the steady increase of the disease and the uninterrupted strain to which they were submitted by their military duties, as well as by the superimposed epidemic, finally brought them to acknowledge the futility of continuing the attack upon such a foe unaided. Indeed, the majority of the small number of Serbian

doctors sooner or later became afflicted with the disease, 126 of them succumbing to it, a mortality of 36 per cent. I recall, very shortly after reaching Serbia, visiting one of the first hospitals I saw where I found six of the seven Serbian doctors sick with typhus. Of the thirteen physicians in the hospital at Pirot, twelve contracted the disease and six died of it. Indeed it was not an unusual thing to find one or more doctors in the different hospitals sick with the disease. In an institution originally reserved for surgical cases with 400 beds, there were approximately 1600 patients, 1100 of which were suffering from typhus. This hospital had formerly a staff of 42, including doctors and their assistants and nurses, and only three of this number remained who were free from the disease. Those physicians who remained well were busily occupied with treating the sick or the wounded from the battlefields, and general methods for prevention throughout the country were impracticable or were not undertaken. There were obviously not enough hospitals in which the sick could be properly cared for or even properly sheltered. Under such conditions, with no efficient sanitary personnel or sanitary regulations, wounded soldiers or those affected with minor diseases or relapsing fever wandered into the hospitals whenever they were so inclined and entered the wards filled with typhus cases, frequently occupying the same beds with them. Indeed, it was exceptional in most of the hospitals to find only one patient in a bed, usually there were two or three patients in the same bed and the available floor space was also covered with patients without beds; sometimes lying upon straw, on blankets, or closely huddled side by side on the wooden flooring, often even under the beds. The conditions in many of these hospitals were about as bad as they well could be. There were no lavatory or bathing or toilet facilities for the patients, no clean linen or clothing for them, and no systematic disinfection of such linen or the beds. There were usually no nurses, and often only a few Austrian prisoners as attendants. Worst of all, during the height of the epidemic many of the patients in the hospitals received no care or attention whatever, for the reason that there was no one at hand to

render it. As the severe type of the disease prevailed with delirium lasting several days, it was sometimes impossible for patients, particularly those in the wards upon the second floor, to visit the latrines outside the hospital. Under such conditions the mortality was naturally great, and reached in some instances as high as 70 per cent. In certain hospitals where patients had removed their clothing upon entrance, I have seen many piles of such clothing lying in the entrance room with thousands of living lice and ova upon the garments not yet disinfested. Indeed many hospitals were without apparatus for sterilizing or disinfesting, or possessed only unsatisfactory appliances for this, and patients came, and left if they recovered, without their clothes being washed or disinfested. In a few hospitals the conditions were so bad that the dead lay unburied for days at a time. The conditions in the prison camps were often worse; the buildings used as prisons were almost invariably greatly overcrowded and insufficiently ventilated. The prisoners were frequently confined in stables also with very poor ventilation. In these there were no wooden floors and they were compelled to lie upon the ground or upon straw sacks or loose straw. The latrines were usually filled to overflowing and in a most unsanitary condition. Inmates of these prison camps I always found very lousy on first inspection. These camps were very dangerous to inspect, and during the war many cases of typhus were undoubtedly contracted in connection with work in the various prison camps.[1] In Serbia they proved to be veritable death traps. It was necessary to institute rigid sanitary reforms in almost every one of these prisons before the disease could be eradicated. Over one-half of the

[1] Low, The Ann. Report, Local Government Board, 1914–15 (xliv) gives a list of sixteen prison camps in Germany in which typhus broke out in 1915, in ten of which British soldiers were confined. "In the camp at Langensalza, in April, 1915, nearly the whole of the 1000 prisoners contracted typhus (Leonetti). It is said that on an average thirty-five men died daily. They were ill-attended, without medicines, and their clothing was insufficiently disinfected. In the camp at Niederzweren typhus also made serious ravages. It was only when the epidemic attacked the civil population and the garrison that precautions were finally taken. At Erfurt there were 600 cases among 20,000 prisoners. In the camp at Gustrow the hygienic conditions were equally deplorable. The 12,000 prisoners, suffering from cold and hunger, were crowded together on mouldy straw, with a single blanket apiece, which was worn, and often torn."

70,000 Austrian prisoners in Serbia died of typhus during the epidemic. The Serbians supplied their prisoners with as good food as it was possible for them to furnish, but the sanitary conditions of the people of Serbia in general precluded the placing of their prisoners under proper sanitary conditions.

In the early part of the epidemic, there were no hospitals for the women and children, so that when they were affected with the disease they were compelled to remain at home or wherever they were taken sick, and hence usually were not attended by physicians. Nevertheless, the mortality among them was frequently lower because they at least received some care and attention from members of their family and were probably usually fed more or less regularly.

In order that the reader may better realize the conditions in Serbia, a few extracts from reports of those who witnessed these scenes will be quoted. Sir Thomas Lipton who did so much for the Serbian people, and whose own health was greatly impaired for a number of months owing to hardship and exposure undergone in Serbia during the epidemic, recounting the conditions there in March, 1915 says:

"I met on the country roads many victims too weak to crawl to a hospital. Bullock-carts were gathering them up. Often a woman and her children were leading the bullocks, while in the cart the husband and father was raving with fever. Scarcely enough people remain unstricken to dig graves for the dead, whose bodies lie exposed in the cemeteries. The situation is entirely beyond the control of the present force, which imperatively needs all the help it can get — tents, hospitals, doctors, nurses, modern appliances, and clothing to replace the garments full of typhus-bearing vermin."

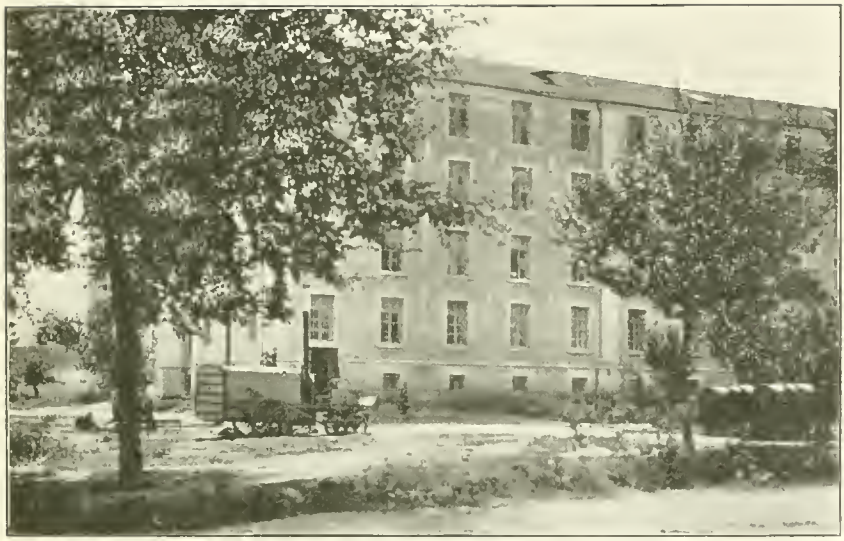
His picture of the hospital at Ghevgheli, where Dr. James F. Donnelly of the American Red Cross died, is appalling. Sir Thomas calls Dr. Donnelly one of the greatest heroes of the war. In his description of this hospital he says:

"The place is a village in a barren, uncultivated country, the hospital an old tobacco factory, formerly belonging to Abdul Hamid. In it were crowded 1400 persons, without blankets or

mattresses, or even straw; men lying in the clothes in which they had lived in the trenches for months, clothes swarming with vermin, victims of different diseases — typhus, typhoid, dysentery, and smallpox — were herded together. In such a state Dr. Donnelly found the hospital, where he had a force of six American doctors, twelve American nurses, and three Serbian doctors. When I visited the hospital three of the American doctors, the three Serbian doctors, and nine of the nurses were themselves ill. The patients were waited on by Austrian prisoners. The fumes of illness were unbearable. The patients objected to the windows being opened, and Dr. Donnelly was forced to break the panes. One of the first things he did on his arrival was to test the water which he found infected. He then improvised boilers of oil drums in which to boil water for use, and he built ovens in which to bake the clothes of the patients, since the hospital was not provided with proper sterilizing apparatus. The street cleaning and hospital waiting was done by Austrians whose numbers were rapidly thinning from typhus and other diseases."

Captain Bennett of the British Red Cross in describing one of the prison camps in Serbia writes:

"It is not a hospital, remember, but simply an area where 750 Austrians have been collected; nevertheless the disease has fallen like a blight upon the camp. At an earlier date one doctor was in charge of this camp, but he is now stricken down by typhus, and various forms of infection of the malady are raging unchecked. Typhus, dysentery, smallpox, and diphtheria have swept over the place with devastating effects. Last week only twenty men out of 750 could stand on their feet. There they lie in utter wretchedness. Here and there one finds a mattress and here and there a little straw, but the bulk of the sick men are stretched out on the muddy ground. Their clothes are foul and alive with vermin which spread the deadly typhus. The silence of the camp is broken only by sighs and groans. A recent visitor noticed a number of recumbent forms covered with greatcoats and found on removing these that five out of the number had already been dead several days. There was



American Red Cross Hospital at Ghevgheli

PLATE I

nobody to remove the corpses. Here and there some poor wretch crawled about on his hands and knees to fetch a cup of water for his prostrate comrade. This was all the attendance which was visible, and the shocking condition of the men and of the ground on which they lie can be imagined. Can any one be surprised to learn that some sixty men die in this camp every day? Every man in this hideous environment and all his comrades who will enter it subsequently are practically appointed to die, unless help comes speedily. Uskub is a veritable valley of the shadow of death. If the tired nurses leave the crowded hospitals for a little exercise and fresh air they are met by a long procession of bullock wagons carrying rude coffins to the cemetery. Sometimes three coffins with unfastened lids rest on the same cart and the bodies of the dead are exposed as the wheels jolt over the rough pavements."

With reference to one of the hospitals he writes:

"It is practically impossible to go near it; so overpowering is the stench in the street outside that nobody who is not compelled to approach the building can bear to be in its vicinity. Details of the interior cannot well be printed."

Dr. Lilian Mary Chesney [1] points out that at the time when she reached Serbia the medical organization there was more or less paralyzed by the magnitude of the task, and cases of typhus were not separated from others. A separation was effected in about a week, the typhus patients alone remaining in her hospital. "The hospital itself was soon much improved in condition. The great difficulty was the sanitary arrangements, cesspools sometimes within the building and sealed up when full being in use. The whole building was pervaded by the smell of overflowing cesspools. The cesspools also overflowed outside into the laundry, which was not a very desirable arrangement, but it did not seem to disturb the mind of the director at all. Coffins were mere open shells and used repeatedly, the bodies being tilted out into the pits on reaching the cemetery."

Dr. Ethan Butler, who was Director of American Red Cross Serbian Unit No. 3, in writing of the evidence leading up to the

[1] Chesney, L. M.: Practitioner, 1916, xcvi, 542.

illness and death from typhus of Dr. Ernest P. Magruder on April 8, 1915, gives an interesting account of the conditions he encountered. Dr. Magruder was one of the five American physicians to lay down their lives in Serbia during the epidemic, the others being Drs. Albert S. Cooke, John M. Kara, James Francis Donnelly, and Leon Weiss. Dr. Butler, describing his hospital, says:

"Only by stretch of imagination could it be called a hospital. As a matter of fact there was only one hospital, worthy of the name, in all Serbia, the Military Hospital at Belgrade. Into this factory, capable of holding no more than 750 patients on a rational apportionment of floor space, had been huddled 1300 wretched beings, in filth indescribable. The majority of these were suffering from badly infected compound fractures, the result of shrapnel. By actual count there were 192 beds, many of which required propping up to keep them on their legs. Of mattresses, blankets, sheets, there were too few. A little corner of the basement, about 25 feet square, filled chiefly by stairways, was serving as laundry, presided over by six very dirty peasant women. Needless to say, it was inadequate to meet the demands made upon it. In another part of the basement was a huge pile of exceedingly filthy clothes from the wards above, and next this were stacked the supplies of food to be served later to patients and staff, after passage through the squalid little shed that was called a kitchen. Water came from shallow surface wells. It was turbid and smelled and tasted badly. Subsequent examination showed evidence of sewage pollution in several of these wells. Excreta, sputum, and pus-soaked dressing were scattered everywhere within and without the building. Vermin, especially the body louse, were omnipresent. The stench of the whole thing was overwhelming. Typhus was present in sporadic cases even when we arrived and caused some anxiety, but it was fully a month before the great epidemic that overwhelmed Serbia broke out. Our units were hard hit. Of the twelve nurses, nine had contracted the disease prior to the end of February: all recovered. Of the six surgeons, four had become infected, and of these one, Dr. James F.

Donnelly, had died. Dr. Magruder and myself had escaped typhus. Dr. Magruder was unremitting in his share of the care of the staff individuals, nor did he spare any efforts regardless of the amount of the exposure incurred thereby."

Later, Dr. Magruder, worn out by overwork, finally contracted the disease and died on April 8. He felt that he was unable to relinquish his duties and did not go to bed until he had been ill for five days. As Dr. Butler has said of him, "He passed out honorably fulfilling the trust imposed upon him by the American Red Cross, honorably upholding in the foreign war zone the ideal of one of the noblest institutions of his native land. A Christian of the true type that feared not to face death that others might profit by his labors."

Dr. M. Jeanneret-Minkine of the French Mission describes pathetically the conditions as he observed them in another part of Serbia. Writing of his hospital in Pirot he says:

"At first, I had Serbian wounded who had become ill, but shortly afterwards, a convoy of 250 sick prisoners, many of them suffering from typhus, arrived and was sent to my hospital.

"I wish to draw attention to the following fact which does great credit to the Serbians: the sick prisoners were provided with beds, whereas the Serbian soldiers suffering from the same disease were accommodated in other hospitals, in which they slept on straw mattresses placed on the bare floor.

"As I already had several cases of typhus exanthematicus in my wards and was anxious to protect them from vermin, I gave the following careful instructions to this effect:

"1. Owing to the absence of a reception room, the patients will be completely undressed in the entrance hall and rapidly conveyed on stretchers, naked, covered with a blanket, to the rooms in which they will receive clean underclothing.

"2. The discarded clothes will immediately be put on a cart and taken out of the town; they will subsequently be spread out on a field and guarded by soldiers, pending their disinfection.

"3. The same day, a steam sterilizer will be built in the yard (the pharmacy could not supply me with sufficient sulphur to proceed by sulphurization).

"The uniforms of all the male nurses were immediately deloused partly in the small autoclave left from the old operating room and partly by boiling in the kitchen boilers. The walls of the rooms were washed with milk of lime.

"The convoy arrived during the night. The weather was appalling, cold and snowy. Notwithstanding that the patients were half frozen, I maintained my instructions, and saw that they were enforced with regard to the first arrivals. Then, being obliged to superintend the removal of the last wounded to the neighboring hospital, I was absent for an hour. During that time, a member of the Administration came along, and, disapproving of my instructions, had the patients with all their clothes on carried to the rooms in which they were undressed.

"The uniforms covered with vermin were only then collected together in the corridors and sprinkled with diluted lysin.

"Result: My wards were immediately infested with vermin. The uniforms in the corridors were literally alive, which gave me the opportunity of studying their biology.

"While I was asking the Administration for an explanation, the Superintendent had the uniforms, still covered with vermin, locked up in the attic. 'We always do so,' said the Chief Administrator, 'but only wait a few days, and everything will be changed.' But all he did was to construct elegant portable W.C.'s. He believed that typhus infection, similarly to typhoid, was carried by fecal matter. This belief cost him his life.

"As regards the steam sterilizer of which I had drawn a plan, and for the construction of which I required bricks, everybody agreed with me about it, but I was nevertheless asked to wait a few days. This was about the end of January.

"During these 'few days,' the epidemic spread with the rapidity and force of a waterspout.

"In my hospital, most of the Serbians and prisoners admitted for bronchitis or enteritis contracted typhus through infection from vermin. Within a fortnight, all the male nurses

became ill and from day to day the virulence of the disease was increased by the rapid transmission from man to louse and louse to man. The mortality increased at an appalling rate. From 15 per cent in the first case, it rose to 50 per cent. In other hospitals of the town it was even worse, the vermin being still more abundant.

"At the end of January, the surgeon of the hospital developed typhus, whilst in the next room his Austrian colleague was becoming convalescent. He however recovered. The same day, a Czech doctor was taken ill and died. Within the next few days, the Superintendent of the hospital, a young physician who worked under my supervision in an improvised hospital, a Polish surgeon whose room I had just moved into, the Chief Administrator of Sanitation, and later, a Roumanian doctor who had taken his wife and children with him to Pirot, became infected. All died one after the other. I myself contracted typhus in March.

"In short, out of 13 physicians working in the town when I arrived, 2 were immunized by a previous attack of typhus, 2 were taken ill at the outbreak of the epidemic and recovered, 8 contracted typhus when the epidemic was at its height, and 6 died within a month. Only one escaped unscathed.

"The disease caused similar ravages among the soldiers. Every morning, cars drawn by small thin oxen conveyed piles of coffins from the mortuary to the cemetery, preceded by priests clad in sacerdotal vestments who appeared utterly exhausted by the ceaseless repetition of the ceremony. The procession was closed by a territorial guard, detailed day after day to this melancholy task.

"I sometimes saw dead bodies piled like pieces of wood in the mortuary. They were buried almost level with the ground owing to the lack of time. Every day, the cemeteries were extended. The long lines of newly dug earth gave one the impression of a field ready for sowing.

"As the number of victims in my hospital continued to increase, I several times attempted a further disinfection, in which I was only partially successful.

"I was unable to obtain my steam sterilizer, the persons who had promised it having died, and although I was my own master as regards the treatment of the patients, I had no power to requisition equipment without authority from the Administration.

"When visiting the wards, I each day saw one or two parasites fall onto my overall, and on inspecting my underclothing, which I did twice every day, would constantly find some. Even the linen brought back from the laundry was not free from vermin. Both my orderlies became infected and I was obliged to allow one of them to lie down near the stove in my bedroom. There was no room for him in the wards and he preferred, not without reason, dying in the streets rather than entering the improvised hospital in the officers' casino.

"As, apart from my already very heavy work, I was obliged to supervise other hospitals in which the regular doctors were sick, dead or inexperienced, I was faced with the alternative of attending to the patients only quite superficially, by distributing antithermics and digalen as had become customary elsewhere, or of seeing only a certain number of cases daily. I decided upon the latter course and then proceeded to select some intelligent prisoners and taught them how to judge a pulse and how to assist their comrades in the disinfection of their mouth and nose, and to make wet packs (maillots). These assistants were each put in charge of a certain number of rooms and given instructions to give massive subcutaneous injections of ethero-camphorated oil to all patients whose pulse commenced to fail. In this way, I was able to give special attention to the serious cases, those passing through the critical period between the tenth and thirteenth day, and depend on my assistants for the others.

"It must be admitted that if the Serbians showed humanity in treating the sick Austrian prisoners on the same footing as their own soldiers, the prisoners working as male nurses gave me great satisfaction by their zeal, courage, and devotion to the Serbians and to their compatriots. Further, when several of these attendants died of typhus, there was no difficulty about

replacing them, although nobody was forced to undertake the work and those offering their services were warned of the danger. However, in a month, my assistants were all convalescent from typhus exanthematicus and were thus immunized.

"At the end of February, the epidemic still continued; yet not a single hospital possessed a sterilizer. A new Administrator was appointed who appeared full of good resolutions, but who lost his nerve from the very first. He was moreover no longer young and, feigning sickness, did not appear until the epidemic had of itself commenced to subside.

"In the barracks the epidemic claimed many victims among the recruits sleeping on the bare floor in the long dormitories, with straw mattresses as pillows. Their doctors made every effort to combat the disease, the whole regiment, squad after squad, being sent to the station of the military hospital reserved for them where they were given shower baths and their clothes disinfected by steam. The vermin however persisting, I concealed tiny bags of paper filled with parasites and ova in the uniforms. When they had been steamed for half an hour at 80° C., I found that the big ones were all dead, but several of the smaller ones revived after being on the skin of a convalescent patient for an hour, on which I had placed them wrapped in a piece of linen covered with sparadrap. In some of the ova, the movements of the air bubbles inside showed that the embryo was still alive. It was therefore necessary to heat the sterilizer to 100° C. and to leave the uniforms in it, less tightly packed, for half an hour after this temperature had been obtained. Moreover, in the larger wards, the recruits who had just been deloused were reinfected by the men who had not yet been disinfected.

"The civilian population did not suffer much from the epidemic, with the exception of the refugees and those in communication with the hospital. Even the peasant women who, although they should have been forbidden to do so, visited their sick husbands on market days, rarely carried infection to their villages as they were clean and fought the vermin. In the town, at the sight of workmen busy painting names on new

coffins, the women sitting outside their doors did not stop weaving and spinning the many colored tapestries which are the glory of their town. And when a group of Czech prisoners organized a concert at which, after the Russian anthem, the Serbian anthem, and the Marseillaise, music by Wagner was played, the hall was crowded.

"I have already mentioned the very important part played by fear in the prognosis of typhus exanthematicus, so will not refer to it again. I wish however to say how much I was impressed by the ease with which one became accustomed to the idea of death, even of death without glory, from infectious disease. We watched our group of physicians and hospital employees rapidly diminish; the merry party round the dining room table was reduced to three, but nevertheless remained optimistic. Without any effort we had become used to the danger threatening us and faced it, smile on lip and joke ever ready, like soldiers at the front. It is a curious psychological phenomenon that the fact of seeing so many people die, causes one to regard death as a very common event, even when it is a question of one's own death. Life is very busy and there is an adversary to be fought; the situation may be likened to an exciting game of checkers which absorbs you and makes you forget all the rest. Also one has faith in one's good star. The reason for that man's death was no doubt because he was afraid; the one over there was no longer young; that other had over-disinfected himself with alcohol, another was too thin or too fat, etc. One even went so far as to believe that typhus would not be dangerous for one's self and was almost glad to contract it in order to find out what it was like!

"And meanwhile, the epidemic continued its ravages. By the end of February, the number of physicians who had died from typhus in the Serbian reserve hospitals exceeded 100, representing almost a third.

"I was obliged to go to Nish and found the hospitals there better equipped than those of Pirot; they were however similarly crowded. I was asked out to dinner by one of my friends and found one of my fellow-students delirious with typhus in a

corner of the room in which we were eating. In the neighboring hospital, another colleague who had come from Switzerland was dying, without my knowing of his illness. In every town the epidemic was raging. In one, as I was passing the cemetery, I saw more than 200 coffins standing out on the snow, waiting to be put in the earth. The heads of the Sanitary Department may have been anxious, but, in Serbian medical circles, a feeling of fatalism and powerlessness prevailed. The Chief of the Belgrade Pasteur Institute, to whom I expressed my amazement at seeing only anodyne measures employed, himself told me that he was counting upon the spontaneous extinction of the epidemic.

"At Uskub, I at last saw a hospital free from typhus. It belonged to an English Mission with a well-trained personnel, beds, a sufficient quantity of linen, and which above all accepted only a limited number of wounded per room and per doctor.

"With this exception, from Ghevgheli in the extreme south to Valjevo in the north, typhus had spread to all the hospitals of which I heard or which I visited. Everywhere, I saw the same leaden-hued faces with an absent or stupid look in the eyes, the some long rows of straw mattresses on which the unfortunate soldiers were huddled together, semiclothed in their uniforms, or again those beds which many doctors did not dare to approach.

"Fortunately, the first line troops did not suffer as much as the others, the febrile cases being immediately evacuated and, an excellent measure, the soldiers and even the officers being forbidden to leave the zone of operation for fear of infection in the towns.

"In March, during the full period of incubation of typhus, I left the country. An international hygiene commission was shortly after appointed. The allied countries then despatched a considerable number of courageous physicians to Serbia. In May and June the cases of petechial exanthematicus were less frequent than in February, and in August there were only sporadic cases. The epidemic therefore appears to be over."

These quotations, together with the descriptions I have attempted to give, it is hoped will convey to the reader some idea of the situation.

Origin of the Epidemic

Such, then, were the conditions which Serbia was facing when the medical authorities, worn out and overwhelmed by the increasing magnitude of the epidemic, became convinced that outside assistance should be asked for. Accordingly the government of Serbia appealed for foreign assistance in combating the disease which was fast rendering her army inert as a fighting machine and bringing about general demoralization of the country. The valiant part which Serbia had played in the history of the war is too well known to make it necessary to emphasize the fact that Serbia was justified in both asking for aid from her Allies in this connection, and in expecting that such aid should be rendered her.

It will be recalled that in July, 1914 Austria-Hungary declared war against Serbia and immediately thereafter launched a severe attack which came as a surprise to the Serbian army and compelled it to fall back. Belgrade, the capital, was bombarded and the government retired to Nish which became the new capital throughout the period of the epidemic. The Austrians, however, did not immediately follow up this first attack and in their subsequent attempts to cross the Danube and the Sava in the vicinity of Belgrade, they were always repulsed. A more severe and concentrated attack, however, was launched later by the Austrians along the Bosnian border, between Schabatz, Valjevo, and Ujitze, the Austrians forcing their way across the Sava and Drina rivers at several points with the object of separating the Serbian armies at Valjevo. This Austrian invasion was pursued with great bitterness and was characterized by many cruelties to the civilian Serbian population. After five days' fighting in the valley of the Yadar the Austrians were, however, repulsed and driven back across the Drina, 20,000 Austrian prisoners remaining in the hands of the Serbian army. In September the Austrians again attacked along the Bosnian border. They were unable at first to make

any material advance, but gradually the Serbian army was compelled to shorten its line and fall back. In November the Austrians attacked and advanced in great force, this time capturing Valjevo. Belgrade had also to be given up, the Austrians occupying on December 2 a line extending from that city to a point about 40 miles east of Ujitze. The situation of the Serbian army was then precarious, it being exposed both on the north and west flanks. However, with great fortitude the Serbians took the offensive again and a few days later they drove the Austrians back through Valjevo and across the Drina and Sava rivers, once more occupying Belgrade thirteen days after its second capture by the Austrians.

Cases of typhus fever had undoubtedly occurred in the Serbian army in October and November, 1914, the infection having apparently been introduced from Albania, but no epidemic resulted. Typhus, however, was present in the Austro-Hungarian army when it invaded Serbia. After the Austrians retreated in December, when the Serbians had reoccupied the invaded territory, a large number of Austrians, both wounded and sick, many with typhus and relapsing fever, were left behind, and these were found living under most unsanitary conditions. It was necessary to confine these and the other prisoners. As there was very little available shelter they were crowded together in buildings where proper sanitary conditions were impossible, and the number of typhus cases rapidly increased among them. Many individuals who came into contact with them were also attacked. This was particularly the case at Valjevo which had been the Austrian military headquarters. It was in this city, situated in the northwestern portion of Serbia, that the disease first began to appear in serious form among the Austrian prisoners, and from them it quickly spread to the Serbians who had reoccupied the territory. With 60,000 prisoners to care for, many already ill with typhus, the newly arrived troops, the refugees and wounded in this district, the available shelter was far from sufficient. Immediate steps were therefore taken to evacuate many of the sick and wounded, both by the railway which leads from Valjevo as well as by the

carriage roads. The Austrian prisoners were also separated into groups, and distributed throughout the country. The seriousness of the situation from a sanitary point of view was not realized; the patients infected with typhus were not isolated but were allowed to go to their homes or were sent to various parts of the country, introducing and spreading the infection to other troops, to households, or to the inmates of hospitals. No quarantine was placed upon the districts in which the typhus cases were particularly occurring, and hence in a very short time the greater proportion of the country was afflicted with a terrible epidemic. The epidemic increased through January, rose more rapidly in February and March, and reached its height in April when the number of cases in the army and civilian population was in the neighborhood of 9000 per day. Those figures are only approximate because when I reached Serbia there were no available statistics of the number of cases or deaths in the various towns throughout Serbia, and only an approximate number of the sick in the military hospitals could be furnished.

Organization

In America the response to Serbia's appeal for aid in combating the epidemic was almost immediate, and as the United States had not yet entered the war the American Red Cross responded to this appeal, and, recognizing the seriousness of the situation, decided to send a sanitary commission, thoroughly equipped with materials and supplies, for the purpose of eradicating the disease, in addition to the hospital units which it had already sent and which were performing such excellent work in connection with caring for and treating the sick. The Rockefeller Foundation was interested in this sanitary commission from the time of its organization, and generously supported it with funds in connection with the American Red Cross. Great Britain, France, and Russia also recognized the extreme gravity of the epidemic and the terrible ravages caused by the disease and sent relief expeditions, though largely from a military standpoint, to help in the situation.

FIG. 1. THE BLACK FLAGS INDICATE DEATHS FROM TYPHUS WITHIN THE HOUSES

FIG. 2. TYPHUS VICTIMS AWAITING BURIAL

PLATE II

Owing to the ravages caused by the spread of the disease, almost complete demoralization had resulted in many parts of Serbia. So many officials had succumbed to the disease that a number of the remaining ones, apparently in the depths of despair and thoroughly discouraged at the appalling conditions and the responsibilities which they had been called upon to face, appeared to be reluctant or unable to even attempt to deal further with the situation. A number of them forsook their offices and remained most of the time gloomily in their residences. Almost every Serbian family was in mourning for some relative or friend, and the black flags outside the houses, the sign of death within, were very common throughout the towns.

One of the most immediate and important problems which confronted me after my arrival in Serbia was that of central organization and control, so that absolute authority over all sanitary matters throughout Serbia could be secured. Owing to the loss through sickness and death of many of Serbia's most efficient physicians and sanitarians, such central control was not being exercised, and no general campaign of attacking the epidemic throughout the country was being pursued, though individual relief and hospital units were already at work in connection with the disease. Under the conditions which existed, and which I have attempted briefly to outline, it could perhaps hardly have been otherwise. When I first arrived in Serbia, the services of several foreign relief units which had arrived were not being employed at all and had not even been assigned stations, and in some instances there appeared to be a diffidence on the part of some of the Serbian sanitary officers in making assignments of the duties of the foreign units and of supervising their work. Such voluntary relief units as were at work, and the majority were performing truly heroic service in treating the sick, were pursuing their duties almost independently of one another, and two units from the same country were found to be working almost side by side with a different plan of action. Such central organization and control of sanitary measures throughout Serbia was,

however, secured through the establishment, with the consent and aid of the Serbian government, of an International Sanitary Commission whose resolutions were immediately enforced when necessary through the Ministers of the Interior and of War. In addition, the Medical Director of this Commission was invested with the necessary authority in sanitary matters and in sanitary reform. This organization was effected particularly through the assistance of M. Pachitch, Minister of Foreign Affairs, M. L. Jovanovitch, Minister of the Interior, Sir Charles des Graz, British Minister, and M. Bopp, French Minister to Serbia. Assistant Secretary of Foreign Affairs, Slavko Grouitch, now Serbian Minister to the United States, and Sir Ralph Paget, former British Minister to Serbia, who had been placed in charge of the medical units in Serbia from Great Britain, were also of very great assistance in bringing about this organization. At my preliminary conferences with some of the Serbian officials, it was feared that this organization might lead to some friction among the Allies, but no appreciable difficulties of this nature were encountered. The commissions finally consisted of Sir Ralph Paget, Commissioner of British Relief Units in Serbia; Colonel Karanovitch, Chief of the Military Sanitary Department, Serbia; Dr. Nikolitch, Commissioner of Health, Serbia; Colonel Sondermeyer, Chief Inspector of Military Hospitals (representative from the Serbian Parliament); Colonel Jaubert, in charge of the French Relief Units in Serbia; and Colonel Solfatero, in charge of the Russian Relief. The Prince Regent Alexander was asked to act as Honorary President, Sir Ralph Paget as Vice-President, Lieutenant Petronovitch as Secretary, and the writer served as Medical Director. The headquarters of this Commission were situated at the war capital of the government in Nish. The country having been divided into sanitary districts, sanitary personnel, or hospital units, sanitary stations and hospitals were assigned or distributed to these.

Fig. 1. Camp of unit of American Red Cross Sanitary Commission

Fig. 2. Professor Zinsser and Dr. Maitland at the Paget typhus hospital

PLATE III

Preventive Measures

The general plan of the campaign against typhus included: general disinfestation of people in badly infected districts; general house-to-house inspection in such districts with removal of patients to hospitals for typhus cases; disinfestation of other inmates of such houses; disinfection or disinfestation of houses from which patients were taken or in which deaths from typhus had occurred; the establishment of quarantine and bathing and disinfesting stations at important points throughout the country; the limitation of railway travel by reducing the number of passenger trains; and the establishment of a system of limited travel permits and of inspection of travelers, only cars with wooden seats with no upholstery being permitted to be run; provision for the cleaning and disinfecting of such cars after each journey; provision for the cleaning and disinfestation of public vehicles, particularly of cabs at the railway stations; the sanitary inspection of restaurants and cafés, and the establishment of regular hours of closing during the day for cleaning and disinfection, and the methods to be employed for such disinfection; regulations for hospitals in connection with the disinfestation of the wards, beddings, and linen, and of the inmates and their clothing; the establishment of free dispensaries in various cities, not only for the treatment of the sick but for the early detection of individuals suffering with infectious disease; a campaign of education with printing and distribution of circulars in the Serbian language regarding the nature of the disease, the manner of its spread, and the precautions to be taken to avoid infection.

After the general plan of the campaign was prepared, it was necessary to have accurate information as to the sanitary conditions and the needs of the different districts in various parts of the country, and it was found to be absolutely impracticable to obtain such information unless an actual visit had first been made to the district concerned. Hence a system of sanitary inspection was inaugurated. Much work of this nature was also

carried on personally by the writer and it involved frequent journeys made in as quick a time as possible.

The usual method employed in these primary inspections was comparatively simple. Upon arriving at a town a conference was called of the prefect, the chief of police, the military commander, and the senior military and civil medical officers for the locality. After this conference, inspections would be made with these gentlemen and a plan made for the carrying out of such sanitary measures as seemed necessary. The requisite sanitary personnel and supplies not at hand were then sent to the district. Almost invariably at a later date reinspection of the district was carried out in order to ascertain whether the sanitary measures in question had been or were being actually carried out in a satisfactory manner.

For the purpose of making these inspections, the Serbian government placed at my disposal a railway car, approximately half of which was fitted up with four sleeping berths, with shower bath and toilet facilities, while the other half served as an office and dining room. Although these quarters were not as palatial as this brief description of them might imply, they constituted as regards disease one of the safest places in which to sleep in Serbia. Attached to this car was a second flat car upon which two Ford automobile trucks were carried. It was necessary to carry these automobiles because the railways in Serbia are very few in number (in fact there are only three main lines) and the great majority of the smaller towns are situated away from the track, often at considerable distances from the stations. When it was necessary to spend the night in the open the second Ford truck was employed to carry tents and supplies.

None of the hotels or inns were safe places in which to sleep before being disinfested or unless one took special precautions in connection with a sleeping uniform, and one enjoyed the luxury of a tent in Serbia whenever there was an opportunity to sleep in one. The Ford automobiles were found to be most useful, particularly because, on account of the very muddy and very bad roads, heavy cars could not be employed. It was

FIG. 1. TYPE OF MOTOR TRUCK MOST SUCCESSFULLY EMPLOYED

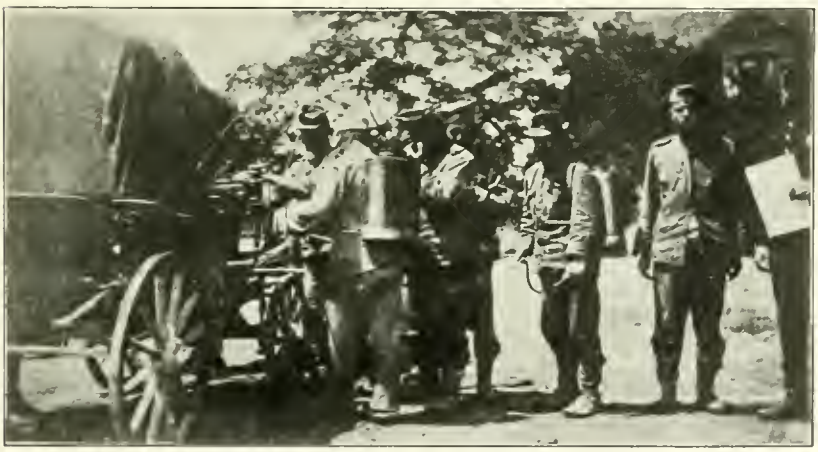


FIG. 2. DISINFECTION OF CARRIAGES

PLATE IV

usually a simple matter, with the assistance of one or two soldiers, to dig out the car when the wheels sank into the mud above the hubs (a not infrequent occurrence) and to then continue upon the journey.

In making the inspections just referred to every effort was made to awaken interest among the people in combating the disease and particularly to arouse to action the officials of the district as well as the people in connection with the prevention of the spread of the epidemic. The Serbian official, though almost invariably good-natured, is often apt to procrastinate in connection with work which requires particular effort or inconvenience, and considerable driving power, initiative, and assumption of authority was often necessary in order to accomplish what was deemed necessary. Obviously it sometimes sorely taxed the patience of a Serbian military commander to be informed, for example, that a certain sanitary measure which required the performance of considerable labor should be immediately carried out, or that other more healthy prison quarters must be found for several thousand Austrian prisoners and certain sanitary measures insisted upon in the new prison. While the authority vested in the writer by the Serbian government was ample enough to secure in the end the carrying out of all sanitary measures considered necessary in connection with the epidemic, nevertheless I have often thought that the natural cordiality and politeness of Serbian officials to a foreigner often accounted for the good-natured manner in which they usually acquiesced in carrying out a piece of work in connection with the epidemic, after they had been thoroughly convinced that there was no other course to pursue.

Occasionally certain sanitary measures of importance were of such a nature (for example, the entire evacuation of certain badly infected districts and the destruction of buildings by burning, or the making of cholera vaccination general and compulsory) as to render the enactment of special ordinances desirable. When such special enactments were desired, they were immediately presented and secured at a meeting of the International Sanitary Commission. The immediate construction of

disinfesting stations and other sanitary measures often required special and immediate expenditure of funds, it being inadvisable to wait for special appropriations from the Serbian Parliament. Funds for carrying on the campaign had already been placed at the disposal of the writer by the American Red Cross and the Rockefeller Foundation, and these were immediately available for emergency work. The writer had also been provided with different funds from private sources which will be referred to later in this Report.

As scientific experiment and evidence have demonstrated that typhus fever is commonly transmitted from man to man by the louse *Pediculus humanus*, and as this disease is commonly transmitted only in this manner, the bathing and disinfesting of large numbers of people and of their clothing in a short space of time was another urgent problem in connection with the Serbian epidemic, and under the circumstances it was imperative to use all available suitable existing apparatus and to hastily improvise all conceivable appliances for disinfestation.

It was very necessary to lay special emphasis upon improvised methods derived from whatever materials there were at hand, as very little perfected apparatus was available or could be secured.

In this connection it should be particularly emphasized that one of the reasons why the epidemic was dealt with so successfully was because the people themselves were instructed and were finally convinced of the fact that the disease was avoidable and that the epidemic could be arrested largely through their own efforts if the proper assistance was rendered them. It was not that the great majority enjoyed taking a bath or being deloused, or having their clothing deloused. In fact, many had not had a bath for over a year; in some instances, their faces betrayed surprise, in others fear, when the water from the shower bath touched their bodies. Many of them desired none of these things, but they submitted to these inconveniences, in fact often welcomed them, and did their part in seeing that they were carried out, solely in order that they might not con-

FIG. 1. EVACUATION OF BADLY INFECTED DISTRICT PRIOR TO ITS DESTRUCTION BY BURNING

FIG. 2. THE USUAL METHOD OF TRANSPORTATION IN SERBIA

PLATE V

FIGS. 1 AND 2. REFUGEES FOR DISINFESTATION

PLATE VI

tract the disease and that the epidemic should be arrested and that they should be freed from the dangers and inconveniences which it entailed.

When I was first asked to go to Serbia to take charge of work in connection with the eradication of typhus, I was strongly advised on two occasions by prominent members of the medical profession against undertaking the work. It was argued that in order to exterminate typhus from Serbia it was necessary to uplift the whole race of Serbian people and to change their entire habits and methods of living and that this would take years to accomplish. At a recent important conference of international sanitarians I heard another physician express a somewhat similar opinion, namely, that before the typhus epidemic in Poland could be put down, it would be necessary to elevate the entire moral tone of the people and their mode of living. I am not in agreement with this idea. I however do believe that such conditions must probably be brought about in a country where typhus has long been endemic if one is to rid it entirely of all its endemic foci of this disease, but experience in Serbia has demonstrated that an epidemic of typhus may be arrested long before an appreciable advance, however desirable it may be, has been made in uplifting the people and changing their entire habits and mode of living. The presence of typhus fever in times of famine, squalor, etc., is obviously particularly due to the fact that among people who are more or less starved, widespread neglect of personal cleanliness occurs and an increased prevalence of lousiness results. The feeding of such individuals and the improvement of their nourishment, however, does not necessarily change permanently their entire habits and mode of life. The epidemic of typhus in Serbia was not accompanied by general starvation or famine and it was entirely eradicated after six months intensive work, but I believe that the habits of the people will show very little permanent change as a result of the measures undertaken. The majority of the people, I think, will not delouse and bathe themselves very much more frequently than they did formerly unless typhus should again visit them in epidemic form, and

they will then undertake these inconvenient and perhaps to many of them disagreeable measures again, not because they are uplifted and their habits of life permanently changed, but because they have been enlightened as to how to avoid the infection and prevent another epidemic.

In the emergency which confronted us in Serbia, it often became imperative, as I have intimated, to improvise on the spot the requisite apparatus for disinfesting and bathing, and makeshift methods of various types were then devised. The majority of these did not attain what might be regarded as high standards of efficiency as disinfestors, but they usually served their purpose in destroying lice and their ova. It is true there were not in Serbia any of the excellent Thresh steam disinfestors on 5-ton Foden steam lorries nor other similar types of perfected disinfestors. Indeed there were very few disinfestors in the country which could be considered of the most modern type. It however was impossible to obtain better types in time for them to be of any value, and therefore their employment was out of the question. All portable steam disinfestors which were present in the country were sought out by means of the sanitary inspections I have referred to above. They were repaired if necessary and all put into regular use. But while the use of the highly perfected steam machines such as the 5-ton Thresh is obviously very desirable in an epidemic, experience in the Serbian outbreak demonstrated that they were not absolutely essential for overcoming the outbreak. One may indeed, when it is necessary, successfully combat typhus with such essentials as improvised baths, clean clothing, fire for producing heat, roughly constructed disinfestors of boards, bricks, and earth, combined with sulphur and petroleum.

In such makeshift work the Serbian people often showed themselves not inefficient. It was frequently only necessary to sufficiently insist that there must be a bathing and disinfesting plant in a district and to give an idea of what was to be accomplished in order for the Serbians to carry out the project in some way, though it was often performed in what today would be considered a very crude manner.

FIG. 1. WOMEN AND CHILDREN ABOUT TO BE BATHED AND DISINFECTED

FIG. 2. AUSTRIAN PRISONERS ABOUT TO BE DELOUSED

PLATE VII

FIGS. 1 AND 2. REFUGEE WOMEN AND CHILDREN, AND MEN AFTER BATHING AND DISINFESTATION

PLATE VIII

Fig. 1. Refugee camp

Fig. 2. Austrian prisoners after being bathed and disinfested

PLATE IX

In view of the immense amount of time and work that has been given to the subject of the construction of disinfestors since the Serbian epidemic, and the number of improved types that have been devised, a detailed description today of many of the makeshift types then employed is hardly justified. Nuttall [1] has recently collected from the literature descriptions of many of the important modern British and some of the German types, and therefore these need not be described here. A few of those employed in Serbia, however, may be mentioned in the present article in order to demonstrate what can be accomplished by such methods.

The most crude and primitive type of disinfestor employed by the Serbian people was made by digging holes upon sloping ground for ovens and lining them with bricks or stones. In these ovens fires were lighted and the opening closed by a wooden cover, or by a metal one if metal was available. After a short time the fire was scraped out and the clothing to be disinfested placed in the oven on a grating and the opening again closed with the cover. The Serbians became very expert in judging the degree of heat requisite to kill the lice and their ova and yet not sufficient to injure the clothing by burning, by placing a piece of white paper in the oven and removing the clothes when the paper showed the first tinge of turning yellow from the heat. Doubtless some of my readers will smile at this crude method of disinfestation, but a very important principle in connection with the suppression of the epidemic was involved by such a practice. It demonstrated that individuals who would really undertake to carry out disinfestation in this patient manner above described, and under such obvious difficulties, were interested in protecting themselves from the disease and thus in putting down the epidemic. Large brick or concrete ovens with double walls of a single brick in thickness between which hot air circulated were constructed and used extensively in many of the smaller villages. In these the infected clothing was loosely placed or hung upon frames. These

[1] Nuttall: Parasitology, 1918, x, 435.

disinfestors, while they were obviously not entirely satisfactory, nevertheless usually accomplished in a crude way the desired purpose.

Another type of disinfestor that was introduced into Serbia by Colonel Hunter and Colonel Stammers, and employed particularly by them in the work of their unit at Kraguevatz and Mladenovac, was termed "the Serbian barrel." The top and bottom of a barrel was knocked out and a grated wooden bottom and a flat wooden lid provided. A short trench was dug in the ground which would accommodate a shallow circular metal tank or boiler with sufficient space for a fire beneath. The metal boiler was placed on two iron bars resting upon the sides of the trench, and it was constructed of the same diameter as the bottom of the barrel which rested upon it. To complete the fireplace in which wood or coal was used, a chimney was sometimes placed at the further end of the trench. After the fire was lighted the clothes were placed in the barrel and the cover held down by a few stones during the process of disinfesting. As Nuttall has remarked, this arrangement might serve as a makeshift but it has drawbacks which need not be emphasized. However, as I have pointed out, it was necessary in Serbia to employ all possible makeshift methods. While the barrel method of disinfestation was nevertheless moderately satisfactory for the individual, it was found to be more desirable to construct, whenever possible, stationary and permanent delousing stations where a larger number of people could be dealt with. Disinfestation of clothing by hot flatirons was employed very little, if at all, in Serbia.

For the disinfestation of very large numbers of people and their clothing in a short space of time, the establishment of sanitary trains was found to be a particularly efficacious method. The disinfection of railroad freight cars and of clothing and blankets in them by steam from the engine in connection with the suppression of epidemic diseases had been employed in Manchuria in 1910 and later in Germany, and freight cars arranged as steam disinfestors were known to be in use in Germany early in the year 1915. The efficacy of the sanitary

Detachment of Serbian army after disinfestation and vaccination

PLATE X

FIGS. 1 AND 2. DISINFECTING UNIT IN CHARGE OF DR. F. GRUVER

PLATE XI

disinfesting train units we employed in Serbia was, however, due particularly to the chief engineer of the Serbian railway service who displayed considerable ingenuity in directing the conversion of the cars for this purpose. As employed by us in Serbia these sanitary train units consisted of three cars, one of which was occupied by a large engine boiler for supplying the steam; a second car, a large refrigerator one, was made air tight, felt being placed at the edges of the side door, and a connecting steam pipe was so arranged that steam from the boiler could be turned into it under low pressure, the ordinary system of pipes in the roof of these cars, finely perforated, being also thus connected up with the boiler engine, the steam passing from these fine perforations downward and through the car. The clothing was hung loosely in the car on wire suspended from hooks. Both lice and ova on the clothing were killed in a very few minutes in this manner, as was shown by repeated tests carried out by Dr. Thomas Jackson, Chief Sanitarian of the American Red Cross Commission. In a third large car shower baths were constructed with a reservoir for water above. These sanitary trains were run upon railroad sidings and large tents were erected near them. The people marched to the tents, several hundred at a time. Usually their hair was clipped, and then, after undressing, their clothing was placed in the steam sterilizing car. They next passed to the car in which the shower baths were placed, and after a thorough scrubbing with soap and water here, they were sprayed with kerosene as an additional precaution for killing the vermin and then received either sterilized clothing or new clothing.

While these units could bathe and disinfest the clothing of a very large number of people in a short space of time, there are so many towns and villages away from the railway in Serbia that other means had to be devised in caring for the people in these localities. In those towns and villages away from the railway, as well as in the large cities, permanent bathing and disinfesting plants were constructed and regular arrangements made for bathing the people by districts, different hours being

arranged for the men, women, and children. Buildings such as factories, warehouses and breweries, and wherever facilities for obtaining steam were available, were particularly employed in forming delousing centres. Where no buildings existed which were suitable for conversion into such plants, these were constructed of rough boards or of bricks, Austrian prisoners being employed for such construction. An attempt was made to arrange for a disinfesting plant of some nature in every town. All the available Turkish baths were used in this connection.

Both the plan of the station and the mode of procedure varied with the facilities available in the locality, and as to whether there were laundry facilities at hand or an existing bathing establishment, or whether shower baths had to be erected. In the hospitals tub baths as well as shower baths were particularly employed, the tubs and much of the piping necessary for the shower baths having been brought from America. These bathing and disinfesting plants were usually arranged so that the infected individuals entered at one side and emerged from the other after disinfestation. There was a room for undressing and another for dry disinfestation, or a shelter under which a steam autoclave was placed and where the clothing was treated; a room for bathing, a room where the individuals were sprayed with petroleum or sponged with carbolic solution, and another where their clean clothing was received and where dressing was accomplished. Sometimes tents were used for the requisite shelter.

Whenever steam was available or a spare boiler could be found, which could be put into use, it was employed for disinfesting clothing. Where steam was not obtainable brick ovens were usually constructed and the clothing disinfested in these. Indeed existing brick kilns were sometimes used for this purpose where available.

For the reason that so many perfected delousing stations have since been described, those constructed in Serbia are also not considered in greater detail.

Fig. 1. Steam bathing and disinfesting unit in charge of Dr. T. W. Jackson

Fig. 2. Men leaving tent before bathing

PLATE XII

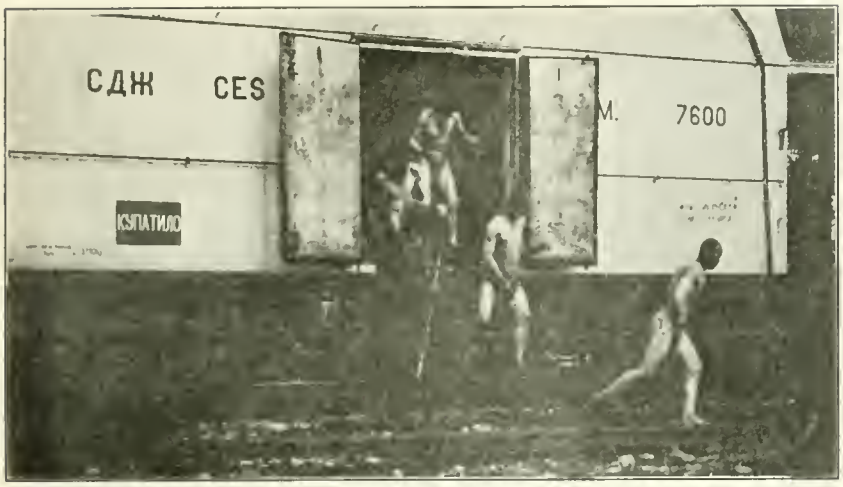


Fig. 1. Leaving bath

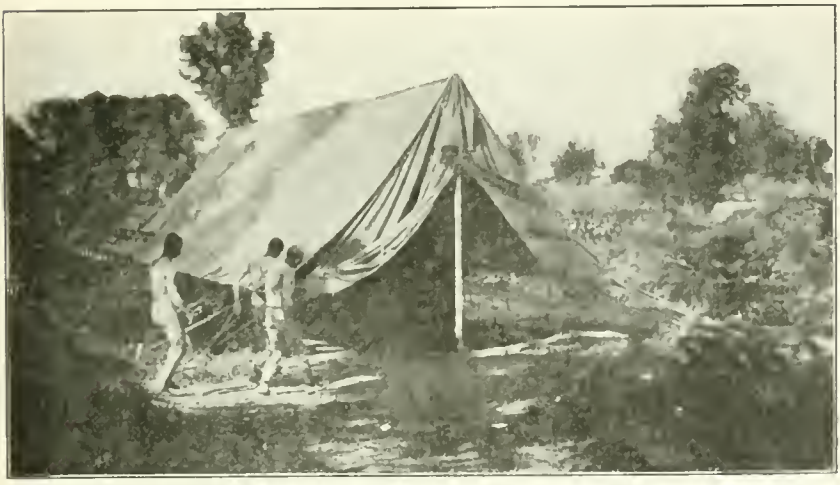


Fig. 2. Returning to dressing tent

PLATE XIII

FIG. 1. CONSTRUCTION OF DELOUSING PLANT WITH AUSTRIAN PRISON LABOR

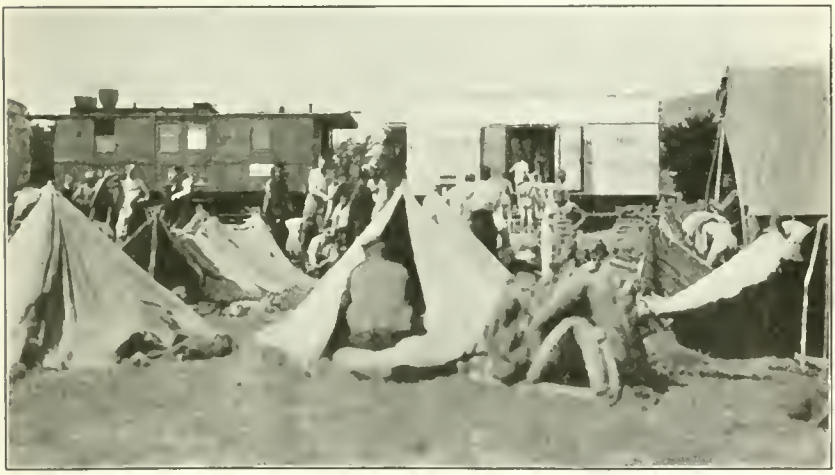


FIG. 2. BATHING AND DISINFESTING UNIT IN CHARGE OF DR. GEORGE C. SHATTUCK

PLATE XIV

Bathing and disinfesting unit in charge of Dr. George C. Shattuck

PLATE XV

As all the hospitals were infected, it was necessary systematically to disinfest these. The patients were first removed from the wards and were placed upon a scrubbing board where they were scrubbed with soap and water and afterwards bathed with dilute carbolic solution. They then received clean clothing and were placed in a ward which had previously been cleaned and disinfested. The wards after being sealed were primarily disinfested by sulphur fumigation in order to destroy the vermin. Then the beds were taken down and after scrubbing with soap and water were treated with carbolic acid solution.

The mattresses and blankets, when there were any, were steamed, and the sheets and other bed clothing boiled. The floors and walls were often scrubbed or sprayed with carbolic acid or bichlorid of mercury solution. In addition the interior of many of the wards was whitewashed.

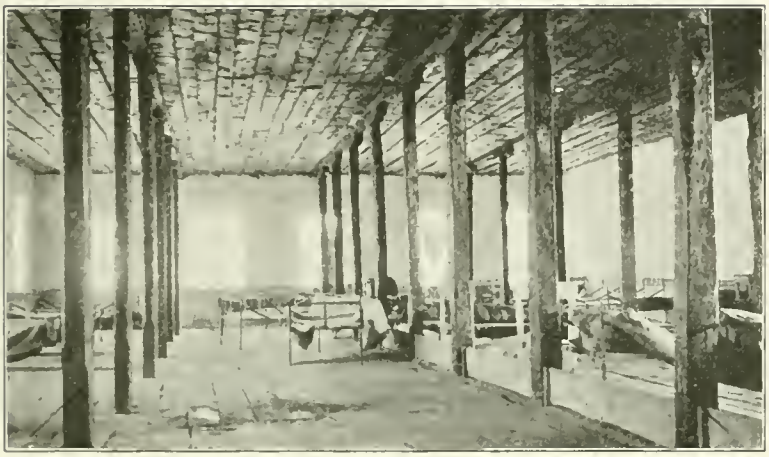
Every precaution was taken to protect the men working in infected places from contracting infection by insisting upon the use of a proper uniform. The Austrian prisoners were largely employed in all this work, and as many of them had already suffered from an attack of typhus and were therefore immune, they were often of particular value.

A uniform which was found to be suitable for nurses and sanitary and medical officers consisted of a one-piece garment, the stockings and trousers combined, to be worn preferably under the outer clothing. A satisfactory uniform should include in addition high boots or shoes, the shoes so constructed as to prevent the entrance of pediculi where they are laced. A wide strip of adhesive plaster should be lightly placed around the leg over the top of the shoe or boot to close the opening. Rubber gloves should be worn when handling infested individuals or clothing, and there should be another strip of adhesive plaster around the top of each rubber glove to prevent the ingress of the lice. It is advisable, for women at least, to wear a closely fitting headdress. The uniform in general should obviously serve to close as completely as possible all openings of the garments and thus prevent access of lice to the skin. Those who come into

very close contact with the patient, and particularly those who examine the throats of patients, until we know more about the methods of transmission of the disease, should wear a simple mask of gauze over the mouth and nostrils, the ends being tied behind the neck. During the recent epidemic of typhus fever in Serbia such a uniform as above described was frequently employed, and some of the physicians employed the simple mask described. When traveling it is always desirable to have with one a folding rubber bathtub and a small supply of powdered naphthalene.

In the anti-typhus campaign in Serbia, heat, whenever it could be employed, was considered by far the most satisfactory means for the destruction of lice and their ova. Although certain experiments seem to show that the virus of typhus fever is destroyed by a temperature of 55° C. for fifteen minutes, and that both lice and their ova are killed by dry heat at 55° C. within fifteen minutes, and also by water heated to 55° C. within fifteen minutes, in our work in the Serbian epidemic, when dry heat was used and thermometers were available to register it, a temperature of about 60° C. for fifteen minutes was regarded as a safer standard to assume for routine practice in connection with the delousing of clothing and blankets. When steam was available for disinfestation it was the custom to submit articles to a temperature of 100° C. for not less than fifteen minutes, usually for half an hour, in order to allow the steam to thoroughly penetrate all parts of the clothing. Fur coats and shoes are obviously likely to be ruined by steam disinfection. However, hot air at 60° C. for half an hour does not injure either furs or shoes if they are dry before being heated to such a temperature. Furs may also be disinfested by carbon disulphid, but this is not recommended for general use and was not employed in Serbia. Shoes may also be disinfested with petroleum.

A great many chemical substances have been recommended for destroying lice and their ova. Those particularly employed in our anti-typhus campaign were petroleum, phinotos oil (a lysol-cresol preparation), sulphur, and to a less extent crude



FIGS. 1 AND 2. PREPARATION AND DISINFECTION OF HOSPITAL WARDS; UNIT IN CHARGE OF DR. FRANCIS B. GRINNELL

PLATE XVI

Fig. 1. Typhus ward after cleaning and disinfecting

Fig. 2. Antimalarial section at work in Macedonia

PLATE XVII

naphthalene and benzene. Spraying with petroleum from a fine spray was rather generally employed after bathing. No injurious effects were observed, and it did not seem to cause much dermatitis in the Serbian people. Petroleum often appears to kill lice within a minute, and does kill them almost invariably within two or three minutes. The ova sometimes survive for a longer period. Some laboratory experiments since performed by Nuttall [1] seem to show that nits are sometimes not killed with petroleum in twenty minutes. In this connection the chemical composition of the petroleum must be considered. The petroleum largely used in Serbia for disinfestation was brought from the United States. Obviously a disinfestant may be shown by occasional laboratory experiments not to destroy all of the ova or lice under the conditions of the experiment, and yet it may be a disinfestant of considerable practical value. Moreover, the very extensive practical use to which petroleum was put in Serbia in connection with delousing enormous numbers of people has shown it to be a very satisfactory disinfestant in connection with an epidemic of typhus. Experimental work on the subject during the war does not appear to have demonstrated a more valuable and more practical disinfestant for the purpose for which it was employed in Serbia.[2] Phinotos oil was particularly employed in the hospitals in a strength of about 2.5 per cent for spraying or washing the bodies of patients after bathing them. Both ova and lice are usually destroyed by this strength of the solution within ten minutes. This preparation in stronger solution, 5 per cent, was also employed occasionally for disinfesting linen and for disinfecting the walls and floors of the houses in which many cases of typhus had occurred, or in the hospital wards where patients were present. Crude carbolic acid was sometimes employed in disinfesting beds. Wards in hospitals and houses regarded as badly infected were first disinfested by sulphur fumigation.

[1] Nuttall: loc. cit.

[2] Castellani and Jackson, from Jour. Trop. Med., 1915, xviii, 253. Kerosene has also been employed with excellent results for disinfestation by the American Public Health Service, Hicks, Am. Jour. Pub. Health, 1917, vii, 628; also Cumming, Jour. Am. Med. Assn., 1917.

Among the American Sanitary Commission were a number of men [1] who had a very wide experience in the use of sulphur with General Gorgas in his campaign against yellow fever in Panama. All the necessary appliances including the sulphur itself, alcohol, pots for burning, paper and paste for sealing, buckets for mixing the paste, brushes, etc., were brought in enormous quantities from the United States. The item of sulphur alone amounted to 100 tons.

Sulphur fumigation in the disinfestation of potentially infective houses and wards during an epidemic, on the whole, is probably the safest and most satisfactory disinfestant for general employment at our disposal. If employed thoroughly and in the proper manner the adult lice are destroyed, and although in a number of experiments in which sulphur dioxid has been employed, all the ova have not been destroyed, nevertheless the chance that in disinfesting a room during an epidemic the few surviving ova are infected and will later develop and still transmit the infection, would appear to be rather remote. Moreover, there is no definite proof that hereditary transmission of the typhus virus occurs in the louse, and the most reliable recent evidence is opposed to this idea.

If the room is large and is not tightly sealed and rendered approximately air-tight, the amount of sulphur dioxid gas generated must of course be increased and the period of exposure prolonged. In Serbia, for general disinfestation by sulphur fumigation, not less than five to eight pounds of sulphur were employed per 1000 cubic feet, the room or ward being carefully sealed up for a period of not less than twelve to twenty-four hours, the time varying according to the nature of the space to be disinfested. Sulphur has been used satisfactorily for disinfestation during the war, particularly in the French and Italian armies, and in the German army.

Crude naphthalene was employed in finely powdered form for individual prophylaxis. It was found convenient to carry the naphthalene about with one in a bottle, and it was often dusted over the underclothing, particularly after inspection of

[1] Drs. Jackson, Caldwell, Gruver, Colonel Gale and others.

prison camps and other groups of lousy men; also over the sheets and pillows in hotels at night. Naphthalene, from a practical standpoint, must also be regarded of considerable value as a disinfestant for lice, though it is well known that it is not an absolutely reliable one, and that it is dangerous to depend too much upon it. Bichlorid of mercury in 1:500 or 1:1000 solution was occasionally employed in cleaning hospitals. It is known that it is not very reliable for disinfestation in connection with lice, as lice sometimes survive for more than an hour upon surfaces upon which a solution of 1:2000 or even 1:1000 of bichlorid of mercury has been previously sprayed.

A great deal of work in connection with other infectious diseases was also carried out in Serbia. As cholera had occurred in places along the border between Serbia and Austria it was deemed advisable to perform vaccination against this disease, and so vaccination trains and parties were also established which went about the country with the doctors and assistants, who inoculated thousands of people daily. Vaccination against cholera and typhoid fever was made compulsory in Serbia. At first my own method of vaccination against cholera was employed, as it has the advantage of only requiring a single inoculation. Later on typhoid and paratyphoid fever became prevalent and a combined vaccine against all three of these diseases was manufactured in our laboratories in Serbia by the method of Professor Aldo Castellani and sent throughout the country for use.

Dr. Castellani was placed in entire charge of the preparation of the vaccines. No cases of cholera occurred in Serbia during 1915. The water supply of many of the towns was also greatly improved, and artesian wells were bored in a number of instances where the water of the vicinity had been condemned as unsafe after it had been examined systematically in our laboratories, apparatus for boring these wells having been brought from the United States. In fact, a systematic bacteriological examination of local water supplies was one of the tasks which was undertaken by our laboratories.

An important problem in the reduction of the amount of typhoid fever and the prevention of cholera was the disposal of human excreta, and a large number of sanitary and fly-proof latrines were constructed throughout the country, particularly about barracks, hospitals, etc. In many cases the cesspools became filled to overflowing, and there was not a sufficient number of hydraulic pumps in Serbia to empty a quarter of them. Our Red Cross immediately supplied, upon my request, a large number of these pumps. The construction of filter beds for purification of sewage was also undertaken in a number of places, and the sanitary condition of some of the cemeteries, where there were numerous shallow pits in which twenty to thirty bodies at a time had been buried and insufficiently covered with earth, was improved.

A campaign for the destruction of the breeding places of flies, in connection particularly with the spread of typhoid and cholera, and of mosquitoes, in relation to the spread of malaria in southern Serbia, was also undertaken.

In regard to the course of the epidemic of typhus in Serbia and the influence of the anti-typhus campaign upon it, it is interesting to refer briefly to the history of the disease in previous epidemics.

Summary of Previous Epidemics

Hirsch [1] states that the history of typhus is written in those dark pages of the world's history which tell of the grievous visitations of mankind by war, famine, and misery of every kind. In every age as far back as the historical inquirer can follow the disease at all, typhus is met with in association with the saddest misfortunes of the populace. From the writings of Corradi we know that typhus fever was epidemic in Italy in 1505, and shortly afterwards spread from there all over Europe. The disease was described more accurately by Fracastori in 1533, and from this date onward its history can be more readily traced. It had evidently also prevailed extensively at an earlier time and with great severity among the Castilian troops

[1] Hirsch: Handbook of Geographical and Historical Pathology, 1883, i, 545.

VACCINATION AGAINST CHOLERA, TYPHOID, AND PARATYPHOID FEVERS BY PROFESSOR CASTELLANI'S METHOD

PLATE XVIII

Troops being vaccinated after disinfestation by train unit in charge of Major Edward Stuart

PLATE XIX

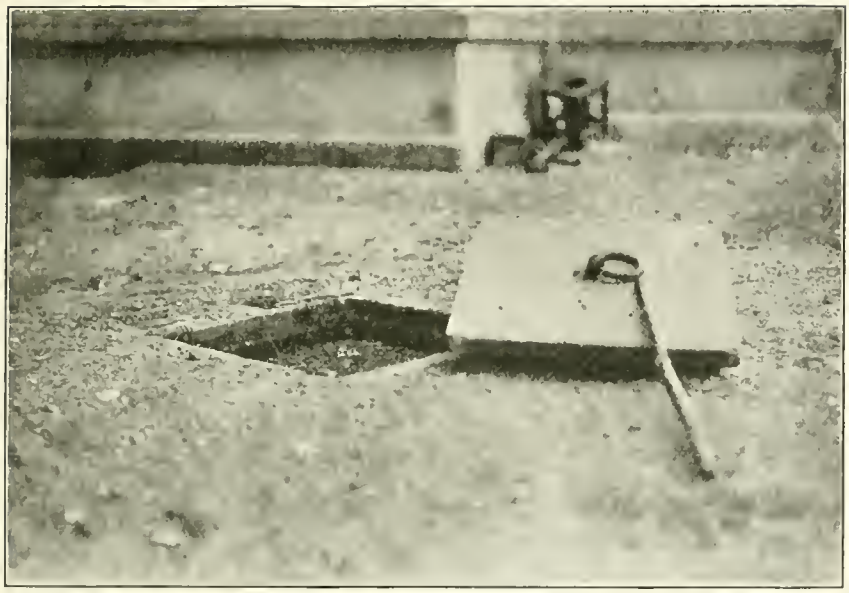


FIG. 1. FILLED CESSPOOL

FIG. 2. A TYPICAL SERBIAN TOWN AFTER ERADICATION OF TYPHUS

PLATE XX

shortly after the siege of Granada. Later (1557) it became known in Spain under the name of *el tabardillo* (the much dreaded red cloak); and in this country there were repeated epidemics. In a third epidemic in Italy in the second half of the sixteenth century, it is said to have destroyed more than one million people in Tuscany. In 1566 it became epidemic in the army of Maximilian II of Hungary and extended its ravages again over Europe, continuing for more than twenty-one years. In the seventeenth century typhus was again one of the diseases which caused the highest mortality. So great were the miseries engendered by it and by the other events in connection with the Thirty Years War, that Haeser, writing of this period with reference to districts formerly well populated, says that one could wander for miles without seeing a living soul, only dead bodies decomposing and partially devoured by wolves, dogs, and vultures, for want of a decent burial. Towards the close of this century Morton implies that practically every hospital in England was filled with typhus victims. The eighteenth century saw no abatement of typhus epidemics, and there is scarcely a year during this century that one may not find references to epidemics of it.

Hirsch, however, distinguishes four periods during which the disease was excessively prevalent; the first period was a continuance of the outbreaks which had occurred in Germany and in Austria-Hungary as a result of the wars waged in those countries. The epidemics died out about the year 1720. During the second period, 1734–44, the disease ravaged Central and Eastern Europe. It was first noticed among the Polish troops engaged in the war of the Polish succession. It spread throughout Russia, Prussia, Silesia, and the central German states and the Netherlands. The English and French troops engaged in these wars were also affected. The third period lasted from 1757–75. It owed its origin to the Seven Years War, starting in 1757 between England and France. The epidemic began in Prussia, extended all over Germany, and then spread to France and Spain. In 1764 and 1767 extensive epidemics occurred over most of Italy, it is said as a result of a total failure

of crops in each case. The fourth and most extensive period began in 1789 in France during the Revolution, and from there spread over the whole of Europe. The disease persisted in epidemic form throughout the duration of the Napoleonic wars, and did not begin to subside until the conclusion of peace in 1815, after the Battle of Waterloo. This was said to be the severest epidemic of typhus fever ever recorded on the continent. The disease was always most severe in those places where the various battles and sieges occurred, but it spread to many places far removed from the sites of war. The general poverty and distress, the results of war, evidently aided greatly in the spread of the disease in these localities.

After this severe epidemic over the whole of Europe no general epidemic occurred until the years 1846 and 1847, when typhus fever became widespread again over the entire continent; however, from 1816 to 1873 in Italy there were fifty-one epidemics, and in France, there were sixteen.

In England there were definite references to epidemics from 1643. According to Creighton, in 1694 the fever deaths in London were 5036. In 1741, during a general epidemic of typhus, there were 7500. Another severe epidemic began in England in 1831, and continued its ravages there for more than ten years, being at its worst, however, between 1837–42. Another serious epidemic occurred between 1862–69, and particularly in London between 1863–65. In England and Wales during the period 1869–83 there were 23,702 deaths from typhus. During 1884–98 there were 2249, while during 1899–1913 there were only 390.

Ireland had long been infected by typhus, and, particularly from 1708, this country was ravaged by one epidemic after another. At the beginning of the eighteenth century the population of Ireland was estimated at about seven million, and during 1846–47 the number of sick at one million, about one-seventh of the population. In Dublin alone there were 60,000 cases of the disease. Since 1815, apart from smaller epidemics, the disease has spread widely six times, the epidemic of 1846–48 above referred to being one of the severest, and the last of these six severe epidemics being from 1862–64.

In Mexico the disease became epidemic in 1530, shortly after the conquest. Another outbreak occurred in 1570, being said to have been imported from Spain. In 1734–36, 189,000 people are reported to have died from typhus fever in Mexico. There have been numerous epidemics during the nineteenth century, one of the most serious in 1861.

In the United States and Canada typhus also prevailed in certain centers in the early years of the nineteenth century, and there were severe epidemics following the Irish immigrations in 1846 and 1847. In South America typhus was probably imported from Spain to Peru at a very early period where it was well known under the Spanish name of *tabardillo* in 1821, 1825, and 1846. It also prevailed in Chili at the same period. The Napoleonic, Crimean, Russo-Turkish, and recent Balkan wars have all been accompanied by typhus. Early in the recent great war, typhus appeared in Germany among the Russian prisoners of war in Austria, and it also became epidemic among the Turkish troops in the Erzeroum district.

It has not been my intention to attempt a complete summary of the history of typhus fever in this Report, but merely to cite many of the important epidemics in order that it may be seen that in earlier years the disease apparently raged almost unrestrictedly. The epidemics often continued for a number of years at a time and were not limited to or by any particular season.

Hirsch writes that out of 147 epidemics which occurred in the temperate and cold latitudes of the eastern and western hemispheres, and of which we have accurate data as to the time of their outbreak and their course, 30 reached their acme in spring, 28 in winter and spring, 21 in spring and summer, 19 in summer and autumn, 18 in autumn, 17 in summer, and 14 in autumn and winter. He concludes that even if there can be no doubt that the maximum of typhus cases falls distinctly in the colder months (winter and spring) yet it is proved that typhus is quite independent of season and weather in its development and epidemic diffusion; that neither the upper nor lower extremities of temperature or moisture can further or hinder the

disease in its breaking out and progress, nor any other condition of weather exert a perceptible influence in these respects. It is in this sense that almost all the authorities express themselves.

Osler has remarked that the gradual disappearance of the disease in Great Britain and on the continent has been one of the great triumphs of sanitation and this also proved to be the case in connection with the epidemic in Serbia. It will be recalled that this epidemic of typhus fever was the first extensive and serious one to occur since the demonstration of the method of the transmission of this disease by lice in 1909–10. It should be emphasized that the efforts of all of the physicians, sanitarians, nurses, and particularly of the people generally in Serbia being directed against the spread of the disease by pediculi, the suppression of the epidemic by intensive work was accomplished within a period of six months.

Method of Transmission

In connection with the Serbian epidemic, it is also important to refer to the method of transmission of the disease.

As long ago as 1876, Murchison suggested, in addition to other measures in connection with the prevention of typhus, that in order to prevent an individual from acquiring such infection, it was necessary to protect him from lice. In 1903, at the International Sanitary Congress held in Paris,[1] Dr. Cortezo made a statement based upon his experiences in an epidemic at Madrid that typhus fever is transmitted by lice and fleas, but no data of specific experiments were supplied demonstrating these facts. It has been for a long time a well-recognized fact that epidemics of typhus fever and of relapsing fever occur side by side and under similar conditions, and the close association of these two diseases has indeed been noted since 1739. This fact and the work carried out upon relapsing fever by Sergent and Foley[2] and Mackie[3] and Smith[4] suggested

[1] Official abstracts of Proceedings of the Conference, p. 343.

[2] Sergent and Foley: Bull. Soc. de path. exot., 1908, i, 174.

[3] Mackie: Brit. Med. Jour., 1907, ii, 1706.

[4] Smith: Medical Thesis (London), 1909, John Bale Sons and Danielson, Ltd.

that lice were also probably the transmitters of typhus fever. However, in 1909, Nicolle [1] working in Algiers showed by actual experiments that the chimpanzee could be infected with the typhus virus by the injection of a small amount of blood from a human active case of the disease. He then showed that lower monkeys could be similarly infected by the inoculation of the chimpanzee's blood, and that then the infection could be transmitted from monkey to monkey by means of the bites of infected body lice (*Pediculus humanus* var. *corporis*). This work was shortly afterwards confirmed in the United States by Ricketts and Wilder [2] and by Anderson and Goldberger,[3] who also showed that the lower monkeys might be infected directly with human typhus blood or by the bites of lice that had fed upon human cases of the disease. Later it was shown by different investigators, Wilder,[4] Goldberger,[5] Prowazek,[6] Sergent,[7] and Nicolle,[8] that the disease may be transmitted to monkeys by inoculating them with the contents of crushed lice or with faeces of infected lice, the lice or their faeces becoming capable of conveying infection from two to eleven days after feeding upon typhus infected blood, and the blood in typhus fever cases being found infective from the third to the tenth day of the attack. A few experiments which have been undertaken with bedbugs and fleas seem to show that these insects do not transmit typhus fever. From other experimental work performed, first by Anderson and Goldberger [9] and more recently by Toepfer[10] Nicolle[11] and others, and from observations made

[1] Nicolle: Compt. rend. Acad. d. sc., Paris, 1909, cxlix, 157; Ann. de l'Inst. Pasteur, 1910, xxiv, 243.

[2] Ricketts and Wilder: Jour. Am. Med. Assn., 1910, liv, 463; Wilder: Jour. Infect. Dis., 1911, ix, 9.

[3] Anderson and Goldberger: Pub. Health Rep., Wash., 1910, xxv, 177; also Bull. Hyg. Lab., U. S. P. H. S., Wash., 1912, Bull. No. 86, p. 13.

[4] Wilder: loc. cit., 1911.

[5] Goldberger: Pub. Health Rep., Wash., 1912, xxvii, 297; and Bull. Hyg. Lab., U. S. P. H. S., 1912, No. 86, p. 37.

[6] Prowazek: Berl. klin. Wchnschr, 1913, l, 2037.

[7] Sergent, Foley, and Vialatte: Compt. rend. Acad. d. sc., Paris, 1914, clviii, 964.

[8] Nicolle, Blanc, and Conseil: ibid., clix, 661.

[9] Anderson and Goldberger: loc. cit., 1912.

[10] Toepfer: Deutsch. med. Wchnschr., 1916, xlii, 1251.

[11] Nicolle: Bull. de l'Inst. Pasteur, 1920, xviii, 49.

by Foster in the Philippines [1] it seems not unlikely that *Pediculus capitis*, the head louse, may also sometimes transmit the disease. Further experimental work on this question, however, would appear desirable. Nuttall [2] apparently inclines to the belief that Goldberger's experiments are not entirely convincing but Nicolle[3] states that *P. capitis* may convey the disease. It has also been suggested that infection may occur in man by the ova of infected lice being rubbed or scratched into abrasions of the skin, but it has not yet been definitely demonstrated if hereditary transmission of the typhus virus occurs in lice, the evidence on this question being contradictory.

There have been no scientific and properly controlled actual experiments performed upon human beings which demonstrate that typhus is transmitted by lice, though Moczutowski in 1900 and Yersin and Vassal [4] and Ostero [5] demonstrated by human experiment that the disease could be transmitted by direct injection of typhus blood. However, in a few instances in which accidental infection or experiments in man were carried out in connection with transmission by lice, the evidence has been in favor of the view that the transmission of typhus is through this agency. These human experiments, however, had not been adequately controlled as is evidenced from the following summary of them.[6]

Sergent, Foley, and Vialatte,[7] trying to prove the transmission of recurrent fever by the louse, made lice who had fed on a patient of recurrent fever bite a man. Another man was inoculated with similar lice, and still another with eggs from such lice. All of them developed typhus. Sergent, Foley, and Vialatte explained this by assuming that the patient was suffering from typhus at the same time or was already infected with typhus. This seems not unlikely, as it is well known that both of these

[1] Foster: Arch. Int. Med., 1915, xvi, 363.

[2] Nuttall: Parasitology, 1917, x, 52.

[3] Nicolle: loc. cit.

[4] Yersin and Vassal: cited by Thoinot, Paris Med., 1915, Nos. 49–50, p. 473.

[5] Ostero: cited by Vincent and Muratet, "Exanthematic Typhus," Univ. of London Press, 1917, p. 207.

[6] Banus: Intern. Jour. Pub. Health, Geneva, 1920, i, 69.

[7] Sergent, Foley, and Vialatte: Compt. rend. Acad. d. sc., 1914, clviii, 964.

diseases occur together in epidemic form, and Kirkovic and Alexieff [1] have reported thirty-three cases in which both diseases were present at the same time, and they state that in most of these cases the recurrent fever appeared first. Another instance of transmission to man is reported by Ussher,[2] who states that a male nurse allowed himself to be bitten by an infected louse and developed typhus in five days. Nicolle, Blanc, and Conseil,[3] tell of the case of the warder in the penitentiary at Tunis who caused infected lice to bite one of two workers coming from the outside and with no contact with any typhus patients. The bitten man developed typhus while the other did not. They describe, too, another case, that of a laboratory assistant who was bitten accidentally by an infected louse and developed the disease. This experimental evidence on human beings alone of transmission of typhus by lice is obviously not strong enough to be entirely convincing and does not exclude the hypothesis of other means of transmission.

A great many physicians of different nationalities have died from typhus during the war and a great many more have contracted the disease. In many instances these physicians were thoroughly cognizant of the method of transference of the disease by lice and of the precautions to be taken in avoiding such infection. In a number of instances where particular care was taken to avoid contamination with lice, nevertheless, infection with typhus followed. For this reason it has been particularly urged that infection sometimes must occur in man by another manner than through the agency of pediculi, and it has been suggested that the droplet method of infection after coughing might sometimes occur in this disease. It is recognized that in the early stages of typhus there are likely to be inflammatory conditions of the mouth, nose, and throat. A number of instances have been recently recorded in medical literature and evidence given which is sometimes in favor and sometimes opposed to the idea of the possibility of droplet infection in ty-

[1] Kirkovic and Alexieff: Arch. f. Schiffs- u. Tropen-Hyg., xxii, 289.

[2] Ussher: Med. Rec., 1914, lxxxvi, 509.

[3] Nicolle, Blanc, and Conseil: Compt. rend. Acad. d. sc., 1914, clix, 661; Ann. de l'Inst. Pasteur, 1910, xxiv, 261.

phus fever. As yet there has been no experimental proof that the sputum or saliva in typhus fever contains the virus, but on the other hand there have been no careful experiments performed upon man in which the saliva or sputum have been employed for infection. Also, even if typhus may sometimes be transmitted to man by droplet infection, the experimental proof of this fact might be very difficult. In this connection we have only to recall the negative experiments performed upon man by Rosenau and his associates [1] in connection with the transmission of influenza by the sputum and by droplet infection. It must be borne in mind that the virus of typhus fever has repeatedly been shown to be present in the blood; that Moczutowski inoculated himself in this manner and suffered an attack of typhus fever after an incubation period of 18 days. Yersin and Vassal also inoculated two men with typhus blood who developed typhus after 14 and 21 days respectively. While the experimental transmission of typhus infection to monkeys and other animals is certainly sometimes very unsatisfactory,[2] and the proof that the infection has been actually transmitted not always definite and convincing without the most minute study, nevertheless, practically all such transmission experiments in animals are also in favor of the view that the virus of typhus is present in the circulating blood and that the blood is usually infected during the active period of the fever. As the virus is present in the blood it would not be surprising if some of the secretions also contained it. The experiments recently performed on man in demonstrating the method of transmission of trench fever are interesting in this connection.[3] A series of inoculations in man with urine or urinary sediments and with saliva or sputum from typhus cases might give further information on this question. While it seems evident that the only common and important method of transmission of typhus is through the louse, and that epidemics of

[1] Rosenau: Jour. Am. Med. Assn., 1919, lxxiii, 311.

[2] See in this connection, Friedberger, Ztschr. f. Immunitätsforsch. u. exper. Therap., 1920, lxxix, 125, who states it is not possible to infect guinea pigs with typhus blood.

[3] Trench Fever, Report of Commission Medical Research Committee, American Red Cross, Oxford University Press, 1918, p. 37.

the disease are due to this method of transmission alone, nevertheless, several careful observers have the impression that exceptionally and rarely typhus may be transmitted to those who come into close intimacy and contact with patients by some other means. In cases of typhus in which there are abrasions of the mucous membranes of the mouth, nose, and throat, the possibility of infection through coughing should be borne in mind. A number of observers are in favor of this idea. Thus Kraus believes that there is some other means of transmission than by the body louse, and states that this was the belief of all the Galician doctors who based their views on the observation that if the rooms containing typhus patients were kept well ventilated, no infection occurred among the personnel. Allan [1] is of the same opinion that, if a person not protected by a previous attack remains some time in a close, stuffy room near the patient, he runs the risk of contracting the disease although no lice may be present. Walter [2] suggests the danger of overlooking such a possibility and describes an epidemic which he could not entirely explain on the assumption of transmission by the louse. Friedberger,[3] in his account of the epidemic in Pomerania, expresses doubts as to whether the louse is the real carrier, because he found cases that he could not ascribe to louse bites, among which were those of four doctors who developed typhus without even having felt a louse bite, and that of a lady who only once for a short time had entered a room occupied by patients in order to give them some apples.

The idea of droplet infection is also supported by Rondke,[4] who bases it on the evidence of the case of one nurse who developed typhus when no new patients had been admitted for ten days, while all the sick people were free from lice. She had taken very carefully all the precautions advised, but did not wear a mask. A similar case is reported by Sellards [5] and Shat-

[1] Allan: Brit. Med. Jour., 1915, ii, 811.
[2] Walter: Berl. klin. Wchnschr., 1915, lii, 851.
[3] Friedberger: Ztschr. f. Hyg. u. Infectionskrankh., 1918, lxxxvii, 475.
[4] Rondke: Med. Klin., 1915, p. 1152.
[5] Sellards: Part III in this Report.

tuck [1] in Serbia of a nurse who protected herself very carefully, wearing a louse-proof suit. She had to sponge and swab the throat of a very severe case with serious lung and mouth complications. The patient was free from lice but coughing frequently. The nurse developed typhus after two weeks. Of the same opinion are Flueggi, Gaertner, Bujwid, Kisskalt, Uhlenhuth, and Stroklosinski,[2] Larrieu and Delarde and d'Halluin. Delarde and d'Halluin [3] believe that in some cases of typhus during the epidemic they studied in Germany, droplets of saliva expelled in coughing were infectious, and when inoculated to the mucosa produced the disease. They also report the case of a physician who was found to be free from lice and yet contracted typhus. One should not dismiss such evidence with the mere statement that the small larval stages of lice may well escape notice. It does not seem entirely improbable that some of the doctors and nurses, who came repeatedly into very close contact with typhus cases and who have lost their lives from this disease during the war, contracted the infection perhaps because they regarded the only possible means of transmission to be by body lice, and only took precautions against this means of infection. That typhus may be sometimes transmitted by some other means than by the louse is a view held by a considerable number of physicians who have had during the war an unusual experience during epidemics, though little credence is given to this idea by some investigators who have no such experience and who have formed their judgment that the louse is the sole transmitter from the louse transmission experiments recorded in the literature.

Granting that the spread of the disease in epidemics is due to louse transmission, and that our methods in combating successfully this disease in epidemics need only be directed against such a means of transmission, nevertheless, it must be borne in

[1] Shattuck, G. C.: Harvard Graduate Magazine.

[2] Flueggi, Gaertner, Bujwid, Kisskalt, Uhlenhuth, and Stroklosinski: Med. Klin., 1915, p. 586.

[3] Larrieu and Delarde and d'Halluin: Bull. et mém. Soc. méd. d. hôp. de Paris, 1916, xxxii, 320.

mind that this does not exclude exceptional instances of infection by other means.

Typhus fever claims more victims in the medical profession than any other epidemic disease. The mortality among physicians in epidemics is generally high. Osler states in a period of 25 years in Ireland, among 1230 physicians attached to institutions, 550 died of typhus. Minkine reports that out of 13 physicians working at the typhus hospitals, 12 contracted the disease, and 6 of them died. Butler in connection with his typhus hospital unit states that of 6 physicians, 4 contracted it and 2 died. The mortality among the Serbian physicians, 126 out of 350, or 36 per cent, has already been referred to. Moreover, some of these physicians were immune from previous attacks contracted before this epidemic. Friedberger,[1] in reporting an epidemic at Schutzen in 1915, states that 24 of the doctors were attacked and 14 died, a mortality of 58 per cent; that of 332 nurses, 71 fell ill of whom 15 died, a mortality of 21 per cent; at the same time the disease among the Russian prisoners showed only a mortality of 7.8 per cent. Why is infection with typhus so common and the mortality so high among physicians? Is there an opportunity of direct infection by some means in which the virulence of the infection (as in pneumonic plague) is uniformly greater than when it is transmitted through the intermediate host, in the case of typhus, the louse; and in bubonic plague, the flea?

Aetiology

Bacteriological investigations in regard to the aetiology of typhus were carried out during the Serbian epidemic in connection with several of the larger hospitals.

In spite of the very large amount of experimental work that has been performed in relation to the causative organism of typhus, there is no general unanimity of opinion upon the nature of the virus. A number of different investigators working in different epidemics in various parts of the world have described species of cultivable bacteria as the cause; others

[1] Friedberger: Ztschr. f. Hyg. u. Infectionskrankh., 1918, lxxxvii, 475.

believe the disease owes its origin to a species of protozoa, and still others think that it is due to a filterable virus.

Rocha-Lima[1] and a number of other investigators regard the so-called *Rickettsia prowazeki* as the cause. Different bacilli, each regarded as specific, have been reported, particularly by Horiuchc[2] in 1909, Ricketts and Wilder in 1910,[3] Plotz, 1914,[4] Rabinowitsch,[5] Arnheim,[6] Rudisjicinsky,[7] Petruschky, 1915,[8] and Zeiss, 1917.[9] Specific cocci have been regarded as the cause, particularly by Wilson, 1910,[10] Proescher, 1915,[11] Penfold, 1916,[12] and Danielopolu, 1917,[13] while pleomorphic organisms (diplococcoid and bacillary forms) have been described by Prejetchensky,[14] Fuerth, Mueller, Hort, and Ingram,[15] and Topley[16] and Gaston.[17] In addition to these claims Futaki (1915)[18] has described a spirochaete, Goldstein[19] a motile diplobacillus, and Milman[20] a non-motile diplobacillus as the cause of typhus. Wolbach and Todd[21] believe that the cause of Mexican typhus fever is due to a new parasite which they call *Dermacentroxenus typhi:* Weil and Felix,[22] Felix,[23] and Friedberger[24] have be-

[1] Rocha-Lima: Arch. f. Schiffs- u. Tropen-Hyg., 1916, xx, 17; Berl. klin. Wchnsehr., 1916, liii, 567.

[2] Horiuehc: cited by Ledingham, Lancet, 1920, i, 380.

[3] Ricketts and Wilder: Jour. Am. Med. Assn., 1910, liv, 1373.

[4] Plotz: ibid., 1914, lxii, 1556.

[5] Rabinowitsch: Berl. klin. Wchnsehr., 1914, li, 1458.

[6] Arnheim: Deutsch. med. Wchnsehr., 1915, xli, 1060.

[7] Rudisjieinsky: New York Med. Jour., 1915, cii, 1175.

[8] Petruschky: Centralbl. f. Bacteriol., 1914–1915, Orig., Abt. 1, lxxv, 497.

[9] Zeiss: Deutseh. med. Wchnschr., 1917, xliii, 1227.

[10] Wilson: eited by Ledingham, Lancet, 1920, i, 380.

[11] Proeseher: Berl. klin. Wchnsehr., 1915, lii, 805.

[12] Penfold: Tr. Soc. Trop. Med. and Hyg., 1916, ix, 105.

[13] Danielopolu: Presse méd., 1917, xxix, 403.

[14] Prejetehensky: Typhus Fever, cited by Cox, Commonwealth of Australia Quarantine Service, 1917, Publieation No. 13, p. 30.

[15] Fuerth, Mueller, Hort, and Ingram: eited by Cox, Commonwealth of Australia Quarantine Service, Publication No. 13, p. 31.

[16] Topley: Jour. Roy. Army Med. Corps, 1915.

[17] Gaston: Revue de méd., 1915, xxxiv, 559.

[18] Futaki: Brit. Med. Jour., 1917, pp. 265 and 491.

[19] Goldstein: ibid., p. 167.

[20] Milman: Jour. Am. Med. Assn., 1915, lxv, 2203.

[21] Wolbach and Todd: Ann. d. l'Inst. Pasteur, 1920, No. 3, p. 159.

[22] Weil and Felix: Wien. klin. Wehnsehr., 1916, xxix, 33; ibid., 1917, xxx, 393.

[23] Felix: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1917, xxvi, 602.

[24] Friedberger: Deutsch. med. Wehnsehr., 1917, xliii, 1314.

lieved that *Bacillus proteus X 19* possesses specific properties in connection with the disease, and Werner and Leoneanu [1] and Hilgermann and Arnoldi [2] have even made human inoculations for protection against typhus with this organism. On the other hand, Nicolle, Hort [3] and others believe that typhus is due to a filterable virus. On account of the attention that has been recently called to the Rickettsia in relation to the disease and the opportunities for the investigation of the actiology of typhus which will undoubtedly occur in connection with the epidemics of this disease in Central and Eastern Europe, it seems advisable to present here a detailed account of the investigations which have been already made in relation to the Rickettsia.

The Significance of Rickettsia in Relation to Disease

In 1916 Rocha-Lima called attention to the presence of very minute bodies which were found in lice which had fed upon patients suffering from typhus fever. These bodies were present not only in the contents of the alimentary canal, but especially in the epithelial cells of the alimentary tract of these insects. He regarded them as very minute microörganisms. They were elliptical, oval, often found in pairs and bipolar in appearance. The smallest forms measured from about .3 to .4 μ and the larger ones, sometimes biscuit-shaped, from .4 to .9 μ. They were best demonstrated by staining in Giemsa's solution. These organisms were not at first found in lice which had not fed upon cases of typhus fever. The lice were said to become parasitized only after ingesting infected blood. Rocha-Lima pointed out that while these bodies slightly resembled bacteria in their morphology, they were in other respects more like the Chlamydozoa-Strongyloplasmata. He therefore proposed for them the name of *Rickettsia prowazeki* (n.g. n.sp.) evidently choosing this name in memory of Ricketts and Prowazek, both of whom succumbed to typhus fever which they contracted

[1] Werner and Leoneanu: München. med. Wchnschr., 1918, lxv, 587.
[2] Hilgermann and Arnoldi: Deutsch. med. Wchnschr., 1917, xliii, 1582.
[3] Hort: Brit. Med. Jour., 1917, p. 265.

while pursuing their independent investigations upon this disease. Subsequently, organisms having a similar appearance were found by other observers and also by Rocha-Lima in lice which had fed upon healthy individuals or on those suffering with various other diseases. For this second form Rocha-Lima proposed the name of *Rickettsia pediculi*. He believes that *Rickettsia pediculi* differs from *Rickettsia prowazeki* in that the former is found normally only in the lumen of the alimentary canal of the louse, and does not multiply in the cells of the insects' alimentary tract, or only does so exceptionally.

It is of importance in considering the study of the Rickettsia to recall that the terms Chlamydozoa (Prowazek) [1] Strongyloplasmata (Lipschuetz)[2] were proposed to include a group of very minute pathogenic organisms or viruses which exhibited certain common properties, while exercising specific peculiarities in each case. These viruses are believed during at least one stage of their development (that of the "elementary corpuscles") to pass through bacterial filters without losing their virulence. Within the cells of the host the elementary corpuscles are believed to grow into larger "initial bodies." The chief characteristics of the chlamydozoa [3] were said to be firstly, their minute size, smaller than any bacteria hitherto known, enabling them to pass the ordinary bacterial filters during one stage of their development; secondly, that they develop within cells, in the cytoplasm or nucleus, and produce characteristic reaction products and enclosures of the cell; thirdly, that they pass through a series of developmental stages and are specially characterized by their mode of division, which is not a simple process of splitting as in bacteria, but is effected with formation of a dumb-bell shaped figure as in the division of a centriole. Two dots are seen connected by a fine line like a centrodesmus, which becomes drawn out until it snaps across the middle, and its two halves are then retracted into the body. In appearance the chlamydozoa seem to consist primarily of merely a grain of chromatin without cytoplasm

[1] Arch. f. Protistenkunde, 1907, x, 336.

[2] Handbuch der Pathogenen Protozoen, Leipzig, 1911, Prowazek and others.

[3] Minchen: Introduction to the Study of the Protozoa, London, 1917, p. 472.

and without a membrane of any kind. Hence they appear to represent the simplest form of living body. The chlamydozoa have not yet been successfully cultivated, but infections can be produced with pure colloid-filtrates free from bacteria, but containing the minute bodies themselves. They are characteristically parasites of epiblastic cells and tissues. The viruses of trachoma, vaccinia, scarlet fever, hydrophobia, molluscum contagiosum, and more recently of typhus fever, have been referred to the chlamydozoa.

Previous to Rocha-Lima's observations, several investigators had published articles describing microörganisms observed in lice which had fed upon typhus fever patients, and Ricketts described a somewhat similar organism in connection with Rocky Mountain fever. It, therefore, is advisable to consider these investigations in chronological order in connection with the discussion of this subject.

In 1909 Ricketts[1] reported upon the occurrence of diplococcoid bodies and short bacillary forms in the blood of guinea pigs and monkeys which had been experimentally infected with blood from cases of Rocky Mountain spotted fever. These organisms were also seen, but not so frequently, in the blood of man. They were also encountered in the female tick (*Dermacentor occidentalis*) and in the eggs of these ticks which had fed upon infected guinea pigs. Ricketts describes his method of examination and the organism itself, as seen in the eggs, as follows: "A number of eggs from the first day's laying were crushed on cover glasses, fixed in absolute alcohol and stained with Giemsa's solution. Each egg was found to be laden with astonishing numbers of an organism which appears typical as a bipolar staining bacillus of minute size, approximately that of the influenza bacillus. Although definite measurements have not yet been made, it is very common to find two organisms end to end with their poles stained deeply. In some instances thousands of these organisms were found, many staining faintly." Morphologically, the organism appeared to him to be

[1] Ricketts: Jour. Am. Med. Assn., 1909, lii, 379, and Med. Rec., N. Y., 1909, lxxvi, 842.

a bacillus, and he points out that its resemblance to the bacillus of haemorrhagic septicaemia is striking, though he was not able to cultivate it. He suggests that the organism in question be called the bacillus of Rocky Mountain fever.

Ricketts and Wilder [1] in 1910 described the organism of typhus fever, which disease they studied in Mexico. In preparations of the blood of patients taken from the seventh to the twelfth day of the disease, stained with Giemsa's solution, they invariably found a short bacillus which had roughly the morphology of those organisms belonging to the haemorrhagic septicaemia group. Usually, this bacillus appeared to stain solidly, but on minute examination an unstained or faintly stained bar was seen to extend across the middle. The exact measurements were not made, but when compared with the size of the erythrocyte, their length was estimated at hardly more than two micromillimeters and their diameter at about one-third of this figure. They also described involution forms of the organism. No active motility was observed in fresh preparations. These bipolar organisms were found in the dejecta and in various organs of lice which had been infected by feeding on typhus patients. While they were also found occasionally in the faeces and intestinal contents of normal lice, they were present almost constantly and often in large numbers in lice from infected individuals.

Gavin and Girard [2] found in the blood of patients in Mexico bacilliform bodies 2 μ in length by 1.2 μ in width, which when treated with Giemsa's solution exhibited at the extremities two small, deeply-stained masses united by a slightly stained portion. They regarded the significance of these bodies as obscure, and did not consider their aetiological significance demonstrated.

In 1913 Prowazek,[3] in the examination of the blood of 51 cases of typhus observed in Belgrade, found that the polymorphonuclear leucocytes showed striking changes. The nu-

[1] Ricketts and Wilder: Jour. Am. Med. Assn., 1910, liv, 1373.

[2] Gavin and Girard: Publ. del Inst. bact. nacional, Mexico, 20 mai et 20 juin 1910; Bull. de l'Inst. Pasteur, 1910, viii, 841.

[3] Hegler and Prowazek: Berl. klin. Wchnschr., 1913, l, 2035.

cleus showed signs of fragmentation and the whole leucocytes became filled with particles of chromatin. These cells stained intensely red with Giemsa's solution and were found to contain numerous rod-shaped and round bodies; diplococcus forms and frequently irregular granules were also observed. At the beginning of the infection many of the leucocytes were free from these bodies, but later more of them contained them. Prowazek, in discussing the nature of these bodies, inclined to the belief that they were related to the strongyloplasmata described by Lipschuetz, which belonged to the chlamydozoa. These bodies tended to disappear during the convalescence of the patient. In addition, he observed in the blood of a number of cases the curious double bodies similar to those first described by Ricketts and Wilder, but he remarks that the significance of these forms is still very obscure. In the examination of sections of organs of typhus cases, trachoma-like bodies were observed in the endothelial cells of the heart, lung, liver, and kidney. Infected lice were carefully examined, and in one case small coccoid bodies and also diplococcus forms were observed.

Sergent, Foley, and Vialatte[1] in 1914 working in Algeria found in lice living only on the sick — never in those living on healthy people or on people suffering from recurrent fever — an organism of which the following description is given: the microbe has the appearance of a coccobacillus. The staining of the poles though never very intense is more pronounced than that of the central portion, which is occasionally quite transparent. The length varies from 1–3 μ and the thickness between .5 and .8 μ. Some of the small forms are shaped like seeds with a diameter of .7 μ. These organisms are frequently seen in pairs. When the germs are abundant they become elongated, forming chains with hardly distinguishable links. They were found in greater number in the bloody fluid of the digestive tract of the lice than in smears of their organs after crushing. The organisms were few during the first days of illness and could be observed only in a small proportion of the lice examined; but their number increased gradually and more

[1] Sergent, Foley, and Vialatte: Compt. rend. Soc. de Biol., 1914, lxxvii, 101.

lice became infected. A number of such lice were fed on healthy individuals and the proportion of microbes seen became much larger. From the twentieth to the twenty-fifth day most of the lice showed signs of infection. The above-mentioned authors did not succeed in cultivating this microörganism on artificial media. They thought the microbe observed by them might be identical with that described by Ricketts and Wilder in the louse. They terminate their remarks with the conservative statement that if the coccobacillus described above does not constitute the virus of exanthematic typhus, it may, however, be supposed that, as is the case in a number of the pasteurella, it is a "temoin" microbe which accompanies the true invisible infectious agent.

Nicolle, Blanc, and Conseil [1] in 1914 found in Tunis the coccobacillus described by Sergent and his collaborators in five per cent of the lice collected in districts which had been free from typhus for two years. In consequence they considered that this germ could not be the agent which produces typhus. They found that lice fed on typhus cases did not become infective before the eighth day, but are constantly infectious on the ninth and tenth days. Two attempts to filter the virus of typhus obtained by grinding up 140 and 155 infected lice both gave uncertain results and therefore they believed that the filterability of the causative agent of this disease cannot be regarded as certain. They could not detect any organism in the blood and organs of guinea pigs infected with typhus.

Proescher in 1915 [2] examined blood smears from nine typhus cases after staining with one per cent solution of methylene-azur-carbonate. Endothelial cells from the blood-vessels were found containing very small diplococci and diplobacilli, measuring from .2 to .3 μ. They were found either singly in short chains or in groups. Very few were seen in the plasma and in the polynuclear leucocytes. These bodies were not found in normal blood or in blood from cases of measles, mumps, scarlet fever, cholera, and relapsing fever. The author suggests that

[1] Nicolle, Blanc, and Conseil: Compt. rend. Acad. d. sc., 1914, clix, 661, and Arch. de l'Inst. Pasteur de Tunis, 1914, ix, 84.

[2] Proescher: Berl. klin. Wchnschr., 1915, lii, 805.

these minute bodies may be the cause of typhus, but he points out as they have not yet been cultivated this fact has not been demonstrated. He believes the nature of the bodies described by Prowazek is still uncertain and states they are smaller than the diplococci and diplobacilli he has found. Whether they are quite different structures or cocci undergoing phagocytosis degeneration products, or granules, is still doubtful.

Dorendorf [1] in the examination of the blood of typhus fever cases in Serbia discovered in all cases examined during the febrile stage of the disease the organisms previously described by Prowazek. These bodies were found in the plasma, in the polymorphonuclear and mononuclear leucocytes, either singly or in pairs. Nuclear variations were a marked feature in the blood picture of the severe cases, and these changes were also seen in the mild cases at the height of the fever.

Stempell [2] in 1916, in dissecting lice collected from sick people, found among the enigmatic parasites brownish bodies in the intestinal epithelium of the louse which he named *Strickeria jungensi* n.g. n.sp. He considered these organisms as the cause of typhus. Coccoid forms encountered were attributed to the same parasite.

Lipschuetz [3] observed in the polymorphonuclear leucocytes in blood from typhus cases bodies like those that Prowazek had described. Of 23 cases examined, 18 were positive and 5 negative. These bodies were not found in control preparations from typhoid fever and variola cases, or in normal blood preparations. He believes that while their nature is obscure they may be of service in the diagnosis of the disease.

Csernel [4] describes the bodies found in typhus blood which seem to be the causal agent of the disease. He gives illustrations of these bodies. They show two distinct phases. One a bipolar bacillus which he regards as the virulent form, and a long bacillus which he believes to be a saprophytic one. In three cases he detected flagella, and was unable to explain their presence.

[1] Dorendorf: Deutsch. med. Wchnschr., 1916, xlii, 345.
[2] Stempell: ibid., 439.
[3] Lipschuetz: Wien. klin. Wchnschr., 1916, xxix, 549.
[4] Csernel: ibid., 1643.

Zollenkopf [1] in describing a new disease resembling intermittent fever (probably Volhynia fever) found changes in the red cells, consisting of blue dots and rods, as many as eight or twelve in a corpuscule. These were not found in preparations taken after the fever, and the author thinks they may be only basophilic granules in the erythrocytes.

Rocha-Lima and Prowazek [2] found during investigations carried out at the Prison Camp, Kottbus, that 95 per cent of the lice taken from sick people were infected by a parasitic microörganism. The organisms were found not only in the contents of the alimentary canal, but especially in the epithelial cells of the alimentary tract. They were not found in lice living on healthy subjects, but on the other hand non-infected lice placed on sick patients became infected with them. Reference has already been made in the beginning of this article to the fact that Rocha-Lima believed that while these bodies were somewhat bacterial-like in appearance, they resembled more closely the chlamydozoa, and he therefore proposed the name of *Rickettsia prowazeki* for them — n.g. n.sp. He believed that this organism could penetrate the cells of the alimentary canal of the louse and multiply actively there. He observed that this parasite has been found in man only in the leucocytes.

Rocha-Lima [3] in another publication points out that in December, 1914, in streak preparations made from lice which had fed on typhus cases, he found large numbers of bacillus-like bodies which stained red with Giemsa's solution. These organisms did not stain well with the usual bacteriological stains. When Prowazek arrived, he recognized that these bodies were the same as those already seen by him in 1913 in a preparation from an infected louse. By the examination of a number of sections of lice from typhus cases, and of normal lice, it was found that the bacillus-like bodies were present in large numbers in the cells of the *alimentary canal* and in the salivary glands of infected lice, but were not present in normal

[1] Zollenkopf: Deutsch. med. Wchnschr., 1916, xlii, 1034.
[2] Rocha-Lima and Prowazek: Berl. klin. Wchnschr., 1916, liii, 567.
[3] Rocha-Lima: Arch. f. Schiffs- u. Tropen-Hyg., 1916, xx, 17.

lice. Of 18 lice taken from a sick patient, 17 were infected by this microörganism. The organism described by him appeared as a coccobacillus which could be easily stained by Giemsa's solution. In the beginning, the parasites were slightly elliptical in shape. Later, during the course of the division they became elongated. The two poles were deeply stained, and joined by a faintly tinted envelope. The organisms did not stain well with the usual reagents, and did not retain Gram's stain. In order to measure the microörganisms, he submitted them to a magnification of 3000 diameters. The smallest forms measured from .3 to .4 μ, while the biscuit-shaped forms measured from .3 to .9 μ. Only a similar picture regarding the occurrence of these bodies in infected lice had he observed up to the present time in normal lice, and not an identical one.

The Rickettsia made their appearance in the cells of the intestine of lice on the fourth or fifth day after they had been placed on the patient, but they did not achieve their complete development before the eighth or ninth day. They developed rapidly at 32° but not below 23°.

Rocha-Lima's experiments with respect to the filterability of the typhus virus did not give positive results, the Rickettsia appearing to remain in the Berkefeld V filter employed. Attempts to cultivate the organism of typhus on various agar media with the addition of ascitic fluid, blood or extracts of the organs of rabbits or of lice were also unsuccessful. He refers to the fact that of all the bacteria described as the cause of typhus, the organism of Plotz might seem to be the most plausible. However, he remarks that the almost entirely negative results with animal experiments in an infection which is so easily transmitted to animals as typhus confirms our scepticism regarding it. He also refers to Petruschky's[1] work, and points out that the organism he has described has only been demonstrated in the sputum, in which the virus has not been proven to be present. He believes that the bacillus described by Arnheim[2] evidently belongs to the pseudodiphtheria group of organisms. He con-

[1] Petruschky: Centralbl. f. Backteriol., Orig., Abt. 1, 1914–15, lxxv, 497.
[2] Arnheim: Deutsch. med. Wchnschr., 1915, xli, 1060.

siders the bodies that he has described are really the aetiologic agents, because he has transmitted the disease to guinea pigs by the injection of lice containing these parasites, and the disease produced was identical to that produced in animals inoculated with the blood of typhus patients.

In a third article Rocha-Lima [1] alludes to the fact that Ricketts and Wilder found polar staining organisms occasionally in the faeces and intestinal contents of normal lice, whereas they found them almost continuously and often in large numbers in similar material from infected lice. In proposing the names of *Rickettsia prowazeki* for this organism as the cause of typhus, he points out that the Gram-positive diplobacillus of Rabinowitsch, the paratyphus-like bacillus of Horiuche, the aërobic, bipolar bacillus of Prejetchensky, as well as the *Bacillus violentus parvus* of Klodnitsky were even more strongly agglutinated with typhus fever serum than the strict anaërobic organism of Plotz. He showed that a louse which was fed upon a typhus patient on the fourth day of the disease showed the presence of Rickettsia infection four days afterwards. This louse was proved infective by animal experiment as well as by microscopical examination, the animal inoculated with it having contracted typhus infection.

In still another publication Rocha-Lima [2] admits that it has not been conclusively proved that typhus fever is caused by *Rickettsia prowazeki*. He, however, alludes to the fact that organisms which are not dissimilar to the Rickettsia and which may be identical have been described in connection with typhus fever by Ricketts and Wilder, by Gavin and Girard and McCampbell in the blood serum, by Prowazek in the leucocytes, and by Rocha-Lima in the blood and organs and in sections. He thinks, however, that the final proof is still wanting that these bodies are identical and are the cause of typhus, and the dimensions given by Rocha-Lima for these organisms are considerably below those given by Ricketts and by Sergent and his collaborators. He believes that the bodies described by Hanser in skin sections from cases of typhus fever are entirely

[1] Rocha-Lima: München. med. Wchnschr., 1916, lxiii, 1381. [2] Ibid., 1917, lxiv, 33.

different from the Rickettsia, and that the organism described by Toepfer in typhus fever cases is not unlike the bacillus described by Rabinowitsch in 1909.

Munk and Rocha-Lima [1] further describe the difficulties in distinguishing Rickettsia from other bodies such as elements of tissue, granulations or coagula, and point out that they can only be identified as microörganisms when in large numbers and when distinctly stained. They believe that it is really impossible even for the experienced eye to identify *Rickettsia prowazeki* by its morphology alone, as has been demonstrated by finding similar microörganisms in lice not infectious. They emphasize that the difference between *Rickettsia prowazeki* and the *Rickettsia pediculi* is that the former develops in the epithelial cells of the stomach and small intestine of the lice, while the latter lies in the lumen of the digestive tube. They point out that the Rickettsia found in lice taken from cases of Volhynia fever and from other patients, or even from healthy people, increase normally in the lumen of the alimentary canal and penetrate only exceptionally into the cells. They remark that Nicolle, Blanc, and Conseil found the same organism in a certain percentage of normal lice, and that Toepfer and Jungmann found the Rickettsia in lice from Volhynia fever cases, and that these Rickettsia also were intracellular. Rocha-Lima and Munk believe that the intracellular Rickettsia are exceptional, except in connection with typhus, and are different from those observed in the lice fed on Volhynia fever cases.

In relation to the microscopical study of the blood in Volhynia fever, they remark that Jungmann, His, Toepfer, and Korbsch thought this disease was due to a diplobacillus, while Toepfer, Korbsch, and Riemer thought the cause was a spirochaete. Rocha-Lima and Munk found diplobacillus-like forms in the blood of Volhynia fever cases, but they also found the same forms in the blood taken from patients with other diseases or even from healthy people. For this reason, Toepfer and the authors came to the conclusion that the bodies described by the investigators named above, and by Jungmann and Ku-

[1] Munk and Rocha-Lima: München med. Wchnschr., 1917, xliv, 1422.

czynski, were probably not the cause of Volhynia fever, and that this link in the chain of proof concerning the Rickettsia as the cause of typhus also is still lacking, particularly since morphologically the bodies found in normal blood cannot be differentiated from those found in typhus blood. Rocha-Lima and Munk were able to transmit Volhynia fever to guinea pigs by the injection of the blood, but not to mice as Jungmann and Kuczynski had done. From this, it would appear that they were not working with trench fever since this disease has not been communicated to guinea pigs. They were able to produce the disease in two guinea pigs inoculated with the urine from Volhynia fever cases, but a bacteriological examination of this urine did not reveal the cause of the disease. The question of the filterability of the virus of Volhynia fever they still consider doubtful.

Munk and Rocha-Lima performed further experiments in cultivation of the Rickettsia, but these were not successful.

In 70 experiments on patients of whom Munk had made the diagnosis of Volhynia fever, 51 gave a positive result with regard to the infection of one louse at least with *Rickettsia pediculi*, 11 remained negative, and 6 were doubtful. Among the negative instances were some typical cases which, although repeated, gave the same results. In 33 control tests of patients whom Munk considered did not have this fever, 26 remained negative, and 6 infected in the same way as the lice from the Volhynia fever cases, while 1 test remained doubtful. These control tests were made on people in the hospital for other diseases, such as malaria, scarlet fever, measles, diphtheria, trichinosis, typhoid fever, tuberculosis, rheumatism, stomach and bladder diseases, and inguinal hernia. The 6 cases upon which the lice were fed, which later were positive for Rickettsia were — 3 with malaria, 1 with bladder disease, 1 with bronchitis, and 1 with inguinal hernia. One who had never suffered from any disease gave rise to particularly strongly infected lice. Among infected lice taken from 14 people, examined at Hamburg, the lice from 2 of these people were found severely infected by a microörganism which

could not be differentiated from *Rickettsia pediculi* either in smears or in sections. One case was undiagnosed. The second was that of a workman who had never been ill, who did not leave Hamburg, and had never been in connection with soldiers at the front. These results confirm those formerly published. In all these cases the intracellular characteristic development of *Rickettsia prowazeki* was absent. The author states that one might think *Rickettsia pediculi* the cause of Volhynia fever, but the fallacy of such an idea is shown by the fact that these organisms have been found in a number of control tests in lice from healthy people in a country free from Volhynia fever. The author admits that it is not impossible that the *Rickettsia pediculi* may be the cause of Volhynia fever, but it is impossible to differentiate this form for the present from that found in lice fed on healthy human beings. Rocha-Lima, however, does not believe that *Rickettsia pediculi* is the cause of Volhynia fever. He states, moreover, that it is only a supposition that this disease is carried by lice. Both Korbsch and himself attempted the propagation of this disease with lice, but their experiments were not successful, although the lice were strongly infected.

Noeller [1] believes in the pathogenic properties of *Rickettsia prowazeki*, though he gives no important evidence of the proof of this idea. He demonstrated in a series of experiments that lice from pigs transferred from infected guinea pigs to pig blood lived long enough for the Rickettsia to develop in them, and that the pig blood was not detrimental to the development of the Rickettsia. He did not think that the infection of the lice was hereditary with this organism.

Toepfer and Schuessler [2] carried out investigations upon about 2000 lice taken from patients. In 400 lice which had fed on 35 patients, bacteria-like organisms were found in the infected lice. These organisms, whose form and appearance they say are characteristic, were constantly present in the intestinal canal of the lice removed from typhus fever patients. They were also often present in the cells of the alimentary tract.

[1] Noeller: Berl. klin. Wchnschr., 1916, liii, 778.

[2] Toepfer and Schuessler: Deutsch. med. Wchnschr., 1916, xlii, 1157.

Control lice fed on other individuals than those suffering with typhus fever remained free from these organisms. From microscopical examination, the organisms seemed to be in pure culture in the infected lice. This organism was found only in lice which had been fed for some days on the blood of patients during the febrile period. Lice fed during the postfebrile period did not apparently become infective. The eggs and offspring of the infected lice were not found capable of producing infection. The parasites continued to develop in the intestine of the lice and apparently remained infective indefinitely. They were not able to cultivate the organism. The injection of the contents of the alimentary tract of an infected louse into a healthy guinea pig produced a febrile condition similar to that produced by the injection of the blood of a typhus fever patient.

In connection with Volhynia fever Toepfer [1] called attention to the presence of characteristic bodies in the blood in Volhynia fever. In three cases of this disease he observed spirochaetes. In one instance, in a fresh specimen, the organism was motile. In lice taken from typhus fever patients he found bodies similar to those described by Rocha-Lima. He is unwilling to commit himself whether a connection exists between these bodies and the spirochaetes.

In another paper relating to Volhynia fever, Toepfer [2] expresses the opinion that the organisms described by His and Werner as the cause of this fever were accidental artefacts. He found in the blood small parasitic-like bodies, but did not consider that these were diagnostic. He, however, convinced himself that the virus was circulating in the blood in this disease as he performed experiments by injecting five cubic centimeters of blood intraperitoneally into guinea pigs and obtained similar temperature curves to those which were injected with blood from typhus patients. He found that lice taken from typical cases of Volhynia fever contained in their alimentary tract bodies similar to the typhus fever organism. These bodies were found both free and inside the cells of the louse, and appeared

[1] Toepfer: Berl. klin. Wchnschr., 1916, liii, 323.
[2] Ibid.: München med. Wchnschr., 1916, lxiii, 1495.

as small short rods. Polar staining rods and diplobacilli forms were present. He believes these organisms to be bacilli and not protozoa, and considers that they are the cause of the disease.

Toepfer [1] in a more recent work examined smears and sections of 500 lice. He believes he has confirmed his former observations regarding the presence of an organism in infected lice. He criticizes the name of *Rickettsia prowazeki* as giving a wrong impression of the nature of these organisms.[2]

He found the same parasite in lice (*Pediculus capitis*) taken from the heads of patients, and he was also able to artificially infect normal lice of this species by placing them upon the sick. Smears made from lice which had previously fed on the blood of patients infected with typhus fever were found to contain nearly pure cultures of the organisms.

In another paper on the aetiology of typhus, Toepfer [3] describes the organism found in tissues of typhus patients and in infected lice as intracellular diplobacilli.

Hanser [4] reports that he has confirmed Toepfer's discovery of bacteria-like forms in the intestinal cells of lice fed on typhus fever patients.

Toepfer [5] in another article upon war nephritis describes similar organisms to those which he had observed in lice fed upon cases of typhus fever or of Volhynia fever. He regards this form of nephritis as a specific disease, probably transmitted by lice. He also considers it plausible that the virus circulates in the blood. Guinea pigs inoculated with blood from the nephritic cases grew lean and had bloody urine, but no rise in temperature. In the lice from the nephritic cases, especially those which had fed during the early stages of the disease, definite bacteria were found almost without exception. He also infected lice by feeding them on the nephritic cases, and in order to control these results he put lice of the same breed upon healthy people and these remained uninfected. These or-

[1] Toepfer: Deutsch. med. Wchnschr., 1916, xlii, 1251.

[2] Rocha-Lima (ibid., 1353) in a subsequent paper controverts the statement of Toepfer regarding the nature of *Rickettsia prowazeki* found in the intestinal cells of infected lice.

[3] Toepfer: ibid., 1383.

[4] Hanser: ibid., 1254.

[5] Toepfer: Med. Klin., 1917, xiii, 678.

ganisms appeared to be identical with those he had found in lice from typhus and Volhynia fever cases. Anaërobic cultures of these bacteria were successful if the contents of the intestine of the lice were placed in dextrose agar, but the colonies were so small that they were of no value for specific reactions. Toepfer thought that the germs of the nephritic cases could be differentiated from those seen in typhus fever by the fact that the latter developed more markedly in the intestine of the lice. He believed that the three different organisms appear in the epithelial cells of the louse. He states that the similarity in appearance between the three forms of bacteria found in lice which he described as the cause of spotted fever, of Volhynia fever, and of nephritis cannot be regarded as an argument against their specificity, because in stained preparations the bacillus of typhoid fever cannot be differentiated from the colon bacillus and several other bacteria. Having found similar organisms in spotted fever, in Volhynia fever, and in nephritis, the author believes that the three diseases, which are clinically so different, belong to the same group. The author thinks that not only from an aetiological standpoint is this true, but that between nephritis and spotted fever there are histological resemblances which he observed in the study of sections of the skin of the oedematous tissue in nephritis cases, a general disturbance of the capillaries being present in both diseases, though in spotted fever the capillaries are much more affected. In the nephritic cases, the kidneys are obviously particularly affected. The author believes that the oedema and nephritis are only partial results of the infection, that the infection extends from the capillaries over the whole body, and that the oedema and nephritis may be entirely lacking in some instances.

In conclusion, he states that he believes that war nephritis is an infectious disease in which several organs are attacked, and that it is caused by an inflammatory and proliferative disturbance of the capillary endothelial cells, and as a result of this a disturbance of the circulation follows.

Otto and Dietrich [1] attempted to confirm the work of Rocha-

[1] Otto and Dietrich: Deutsch. med. Wchnschr., 1917, xliii, 577.

Lima in relation to the Rickettsia to typhus fever. Lice enclosed in small cardboard boxes were covered with a fine layer of gauze and then placed on the under surface of the arm or inside the thigh of typhus fever patients at various stages of the disease and for various periods. The lice placed on the patients during the febrile period became infected from the fourth day, 70 to 80 per cent being infected if they were allowed to feed during the period of seven to eight days. Of these lice placed on the patient towards the end of the disease, only a few became infected. The infection was never found to be hereditary. In addition to the usual bipolar staining organisms found, they also observed short, rodlike, and long, filamentous forms. The threadlike forms were noted in the case of a louse taken from a patient on the fourth day, and were absent in lice which had fed for nine days. They suggest that these forms may be transition stages in the life history of the parasite. They succeeded in infecting lice with Rickettsia by feeding them on a case of typhus fever without the exanthem. Attempts to transmit the infection to guinea pigs by the injection of the gut contents of infected lice were only successful in a small percentage of the experiments. The authors endeavored to prove by agglutination tests with the serum of typhus cases and an emulsion of the gut contents of the infected lice, that the *Rickettsia prowazeki* is the causative agent of typhus.

Wolbach[1] in the study of Rocky Mountain spotted fever points out that the essential lesions of spotted fever are found in the vascular system and that bacillary bodies are present in large numbers in the endothelial cells of guinea pigs infected with the virus of Rocky Mountain spotted fever through the bites of infected ticks. These bacillary bodies had some of the characteristics of those previously described by Ricketts. The endothelial cells accumulate in the vessel walls and around vessels and in the lymphatics. The organisms are diplobacilli in character and show polar staining. The staining, however, is not that commonly seen with most bacteria, and indicates

[1] Wolbach: Jour. Med. Research, 1916, xxxiv, 121.

that the organisms have some of the characters of spirochaetes. All attempts at cultivating them have so far failed. In another paper Wolbach [1] reports the presence and distribution of this organism in experimentally infected ticks (*Dermacentor venustus*, Banks). In the infected ticks, parasites were found similar to those previously observed in the tissues of monkeys and guinea pigs, but never in non-infected ticks. The parasites were present most abundantly in the striped muscle, also in the malpighian tubes, salivary glands, and ducts and brain ganglia. They were numerous in the muscle fibers of the uterus and vagina, and have been seen in the spermatozoa.

In a third paper Wolbach [2] gives the characteristics of these bodies as follows: "In guinea pigs and monkeys, in sections, a minute rod in pairs, often lanceolate and surrounded by a clear zone or halo and staining with difficulty, occurring in large mononuclear cells (endothelial cells) and smooth muscle cells. Larger and smaller forms were mentioned, the former lanceolate, the latter occurring in smooth muscle cells. In smear preparations from guinea pigs there were noted lanceolate paired forms, rods with irregular staining, and rods with chromatoid granules.

"In ticks, in sections (1) a lanceolate paired form, (2) a smaller, more slender rod-shaped form, and (3) a minute, oval-coccoid form; in size, just within the limits of resolution with the best optical equipment."

He also describes in this last paper the presence of these bodies in the lesions of the blood-vessels in fatal human cases of Rocky Mountain spotted fever, and thinks they are forms of a new organism.

Lopez [3] in a study of the blood in typhus fever found the intraleucocytal bodies discovered by Doehle [4] in cases of scarlatina and also recognized by Preisich and others in different diseases. Lopez found these bodies in 77 out of 90 cases

[1] Wolbach: Jour. Med. Research, 1916, xxxv, 147.

[2] Ibid., 1918, xxxvii, 499.

[3] Lopez: Bol. de la Direction de Estudios Biol., 1917, ii, 92 (reviewed in Trop. Dis. Bull., 1918, xii, 108).

[4] Doehle: München. med. Wchnschr., 1912, July 23, No. 30.

of typhus fever examined by him. From one to three bodies were found in one leucocyte, and the percentage of leucocytes always polynuclear containing them varied from 3 to 80 per cent. They were best stained by Giemsa's method. He remarks that the blood must be taken from well-marked cases of the disease and at the height of the fever from the sixth to the tenth day to contain these bodies. He thinks that they may be chlamydozoa, but does not express a decided opinion regarding their nature.

Schmidt [1] found in three patients only out of many cases of five-day fever examined, almond or sickle-shaped organisms in the blood which showed one or two round chromatin bodies in the interior, situated either peripherally or centrally. They were best demonstrated by Giemsa's stain. The size varied, but is comparable with that of blood platelets.

Jungmann and Kuczynski [2] found in the blood of typhus patients during the first days of the rash an organism which they believe to be identical with *Rickettsia prowazeki* which they had also found in cases of trench fever. As they had never found this organism in other diseases, they conclude there must be a relation between typhus and trench fever.

Werner and Benzler [3] in examining lice which had fed upon cases of *febris quintana* found in the stomach of some of them organisms resembling spirochaetes. In one, the stomach contents of the louse showed bodies which could not be distinguished from those described by Rocha-Lima in typhus and by Toepfer in *febris quintana*, and which had previously been cultured by him anaërobically.

Brumpt [4] studied 72 body lice (*Pediculus corporis*) taken from prisoners of war who had been living in France for some time, and whose state of health was quite satisfactory. No case of typhus fever had ever been reported among them. Twenty-seven lice from the head (*Pediculus capitis*) taken from a healthy child at Rennes were also studied. Of the 72

[1] Schmidt: Deutsch. med. Wchnschr., 1917, xliii, 682.

[2] Jungmann and Kuczynski: Ztschr. f. klin. Med., 1917, lxxv, 251.

[3] Werner and Benzler: München med. Wchnschr., 1917, lxiv, 695.

[4] Brumpt: Bull. Soc. de path. exot., 1918, ii, 249.

body lice from 7 healthy prisoners of war, 53 were found infected by the microörganism described by Rocha-Lima under the name of *Rickettsia prowazeki*, and considered by him to be the causative agent of typhus fever. Of the 53 lice with parasites, 18 were considerably infected. Their alimentary canal and a number of the cells contained what may be described as a pure culture of the microörganism in question. In the 35 remaining instances, the infection was slight. *Herpetomonas pediculi* was not observed. Brumpt's investigations are so important that it is advisable to consider them in greater detail. A group of 16 lice taken from healthy prisoners of war were all found to be infected with Rickettsia. Infection was marked in 1 case, moderate in 13, and mild in 2. Twenty-four lice taken at the same time from these same men were fed upon the author himself once a day for three days and kept in the incubator at a temperature of 20° C. After the third day the surviving lice were dissected, and the following results were obtained: severe infection was found in 5 cases, moderate infection in 5, slight infection in 3, and no infection in 7. Lice from another healthy prisoner were fed upon the author. Thirteen of these surviving lice were dissected, when 1 was found to be strongly infected, 5 moderately infected. In 2 the infection was slight, and 5 showed no signs of infection. Eighteen lice taken from another healthy person were fed on the author. In 4 of these, intense infection was found, in 1 moderate, 2 slight, and in 5, no infection was present. Lice were taken from another healthy subject and fed on the author. Of the 6 lice which survived, 5 showed severe infection, and 1 no infection. Lice taken from another healthy prisoner of war were fed on the author for four days. The 9 surviving lice were dissected with the result that in 2 instances a severe infection was present, in 2 a moderate one, and in 5 no infection was found. The microörganism in question was found practically as a pure culture in the dejecta of the louse. No sign of infection was found in the alimentary canal of 27 head lice taken from a healthy child. The germs found in 73 per cent of the lice taken from healthy individuals were either elliptical in shape, occasionally spherical, but

generally coccobacillary in form. There is always a predominating shape in the Rickettsia encountered in one louse. They are either practically round or slightly elongated. The organisms stained like spirochaetes in the blood. They showed intensely tinted poles, joined by a faintly stained central portion. The average dimensions of the organism varied between .4 and .6 μ for the round forms, 1.2 to 1.4 μ in length, .5 μ in width for the average forms, 1.65 μ to 2 μ long by .6 μ wide for the largest forms. The last were seldom met with. The author never observed the parasites in chains. He concludes that his observations lead him to identify the organisms found in lice taken from healthy people with those previously described by Rocha-Lima under the name of *Rickettsia prowazeki*. Seventy of these lice were fed upon himself and 53 were found infected with the above described organism; but he remained healthy. The author points out that although this organism in question which has not been cultivated may be encountered in the blood or in the organs of some of the patients, it need not for this reason be considered the pathogenic agent of typhus fever as it may have been inoculated by the louse and have no pathogenic action. The author points out that the lice infected by the coccobacilli retain the infection during their entire life. The lice carrying the typhus virus are active from the eighth to the tenth day.

Arkwright, Bacot, and Duncan[1] reported that in their investigations they used a clean stock of lice bred in captivity and kept under observation for over three years. They fed these normal lice on trench fever patients both during and after febrile periods. Either the feeding on the infected person was for one day only, followed by feeding on a healthy man, or after the first infecting meal the lice were fed regularly on the same or another infected man, and between the feedings the lice were kept in an incubator at a temperature of about 27°C., or in an inside pocket. They were later examined microscopically either by films made from the excreta, or from the gut contents, or in microscopic serial sections. The films were

[1] Arkwright, Bacot, and Duncan: Brit. Med. Jour., 1918, ii, 307.

treated with acid alcohol to fix and to remove haemoglobin débris, and were then stained with Giemsa's solution. The following conclusions were reached by them, confirming and extending the work of previous workers:

1. If a box of lice is fed on a trench fever patient, and the excreta collected after a period of about ten days, large numbers of Rickettsia bodies can almost invariably be found in films. Smears of the guts of lice from such a box contain large numbers of these bodies after about the same interval of time. Of 253 specimens from boxes of lice which had been fed on trench fever patients at least five days previously, 150 showed Rickettsia bodies, 83 gave a negative result, and 20 a doubtful result.

2. The excreta from sixteen boxes of lice which were examined daily after an infecting meal showed Rickettsia bodies for the first time twice on the fifth day, three times on the seventh, three times on the eighth, four times on the ninth, three times on the tenth, and once on the twelfth day from the first infecting meal. When first seen only small numbers were noted in the films, but three or four days later enormous numbers appeared. These experiments show that after an infecting feed there is a period during which these bodies are not recognizable on account of their small numbers, or of some difference in form. When a box has once become infected with Rickettsia the excreta collected from it continue to show the bodies for two or three weeks, or till the lice which partook of the infecting feed are dead.

3. All lice from an infected box do not show Rickettsia; only a small proportion do so in the first week; the proportion increases until after two and a half to three weeks the great majority show these forms. Experiments at Hampstead have also made it probable that after the same time a considerable proportion of lice are infective.

4. Trench fever patients can infect lice with Rickettsia bodies during the fever, between the attacks, or even several weeks after an attack during a non-febrile period.

5. Normal lice, fed on persons who have not been exposed to

trench fever infection, have remained free from Rickettsia. Of 245 specimens from 22 boxes fed on seven healthy persons only one specimen of excreta was found to contain forms which closely resembled Rickettsia microscopically. It is not surprising, considering the difficulty in recognizing such small bodies by their morphology, that occasional errors should occur. Four other specimens from two boxes showed these bodies, but they were being fed on a man who had been working with infected excreta in the laboratory for five weeks, and had also been feeding infected lice on himself for the same period. He developed trench fever three days after that upon which the first one of the four positive specimens was found. It is most probable, therefore, that he had been infected for some days before the bodies were observed in the lice.

They further pointed out that Rickettsia bodies are very small and approach the limits of filterability of a Berkefeld filter. In their experiments the Rickettsia bodies did not make their appearance in lice till about the fifth to the twelfth day after an infecting meal. In 53 experimental inoculations of volunteers, the lice or excreta of lice used as the virus were also examined microscopically. In every case the lice had previously been fed on a trench fever patient. Twenty-seven of the specimens showed Rickettsia bodies and caused trench fever; 10 specimens did not show Rickettsia bodies and did not cause trench fever; 1 specimen showed Rickettsia bodies but did not cause trench fever; 2 specimens did not show Rickettsia bodies but caused trench fever; 4 specimens gave doubtful results microscopically, or the inoculation was followed by fever of a doubtful nature; 9 specimens showed Rickettsia bodies but did not cause trench fever. The authors thought this was because the virus had been heated or treated with disinfectant, or because the volunteer inoculated had recently passed through an attack of trench fever and was probably immune. They believe the agreement between the demonstrable presence of the virus and the Rickettsia bodies is very close, and that a very close correlation has been shown to exist between the presence of Rickettsia bodies in lice or the excreta

of lice and the virulence of these materials when inoculated into man.

Most of the observers so far mentioned in this article, who have regarded the Rickettsia as representing microörganisms, apparently have believed that they were either chlamydozoal or protozoal in character or at any rate were of a non-bacterial nature. Other investigators, however, have believed the bodies described as Rickettsia are really bacteria, and more recently it has been suggested that the bacillary forms are identical either with the bacillus described by Plotz as the cause of typhus fever or with the *Bacillus proteus X 19*, believed by others to be the cause of this disease.

Rabinowitsch [1] in 1914 refers to the fact that in 1908 he discovered the causative agent of typhus naming the organism *Diplobacillus exanthematicus*. In fresh cultures the organism practically always appeared as a diplobacillus. Degeneration forms only developed in old cultures. In fresh cultures, the organism was always Gram-positive, while in old ones it became Gram-negative. Cultures were best obtained the author says by using a medium consisting of equal parts of ascitic broth mixed with 4 per cent glycerin. One hundred c.c. of this mixture were to be inoculated with from 3 to 5 c.c. of the blood of a typhus patient obtained shortly before the crisis. After the crisis the organism seemed to disappear from the blood. He points out that guinea pigs can be infected both by the injection of cultures and by the blood of typhus patients, the incubation period varying from 5 to 37 days. He examined the blood of 58 typhus patients. In the films stained deeply with Giemsa's solution he found peculiar, very deeply staining leucocytes which had a very basophilic protoplasm. They often constituted from 3 to 8 per cent of the white cells. He thought that these might furnish a means of diagnosing the infection.

Mueller [2] made bacteriological examinations of various cases of typhus occurring amongst the Bosnians in the Marine Hos-

[1] Rabinowitsch: Berl. klin. Wchnschr., 1914, li, Part 2, 1458.

[2] Mueller: München. med. Wchnschr., 1913, lx, Part 1, 1364.

pital of San Bartolomeo, Trieste. In Giemsa-stained preparations, diplococci, cocci, and ovoid rod-shaped bodies were found present in the blood of all the cases of typhus examined, and also in four patients that no longer showed any fever. The cultural examination of the blood of eleven patients gave five positive results, in each case a diplobacillus developing in the broth. Attempts to cultivate the organisms on ascitic agar succeeded only three times. The isolated cultures seemed to be identical with those obtained by Fuerth from cases of typhus in Tsingtau. The organisms were non-motile rods which readily round off into coccoid forms in the various culture media. The pathogenicity of the culture organism towards animals was only very slight. When mice were inoculated with enormous doses, they succumbed within 24 hours, and the diplobacilli were found in every part of the body. A rabbit showed a single parasite after an incubation period of seven days. On the other hand, three monkeys inoculated with the cultures remained normal. According to the author there can be no doubt that this diplobacillus isolated at San Bartolomeo is identical with the organism described by Rabinowitsch and others.

Olitsky, Denzer, and Husk [1] state it is their opinion that the *Bacillus typhi exanthematici* described by Plotz corresponds to the organism described by Rocha-Lima as *Rickettsia prowazeki*. They point out that while Rocha-Lima found the Rickettsia to be Gram-negative, and that the bacillus described by Plotz was Gram-positive, that the organism described by Plotz may be sometimes Gram-negative [2] in the first subcultures made from lice or in smears made directly from typhus infected lice, as has been shown by Baehr and Plotz,[3] and Baehr and Plotz have reported the occurrence of the Plotz organism in infected lice and have grown it under anaërobic conditions. They have also produced typhus fever by the injection of infected lice. For these reasons they think the Rickettsia and the Plotz bacillus are identical. They think the

[1] Olitsky, Denzer, and Husk: Jour. Am. Med. Assn., 1917, lxviii, 1165.

[2] Baehr and Plotz: Jour. Infect. Dis., 1917, xx, 201.

[3] Olitsky, Denzer, and Husk: ibid., 1916, xix, 811.

reason that the bodies described under the name of Rickettsia have not been cultivated by other observers is owing to the fact that improper methods have been used. Popoff [1] believes that the *Rickettsia prowazeki* described by Rocha-Lima is the same organism as the bacillus described by Plotz as the cause of typhus fever.

Kuczynski [2] carried out his experiments with a view to determining the rôle played by *Bacillus proteus X 19* in typhus fever. Seventy-two body lice were artificially infected with a pure culture of this organism. After examining the lice which survived for 72 hours, he came to the conclusion that *Bacillus X 19* and Rickettsia are not identical, and that it is possible that infection with Rickettsia prevents the development of *X 19* under natural conditions. He found that *X 19* developed in the louse and believes that the rod and threadlike forms described by other authors as developmental stages of Rickettsia are probably stages in the development of *X 19*. He fed these experimental lice upon himself and as he remained healthy he came to the conclusion that *X 19* is not pathogenic. In another paper [3] he made histological investigations upon material from typhus fever cases.

In the petechiae of typhus he was not able to find anything which appeared definitely to be the causative organism. In the investigation of sections of the liver in the endothelial cells of the capillaries and in free phagocytic cells, two different microorganisms were found. First, large bacilli-like bacteria which appeared similar in appearance to the proteus bacillus; and second, bodies in sections stained by Giemsa's solution, resembling the Rickettsia as described by Rocha-Lima in the intestinal cells of lice. The author believes he could differentiate these bodies from other histologic elements by their intracellular position, their spherical grouping, and their intensive stain.

[1] Popoff: Med. Klin., 1917, No. 14, p. 397.

[2] Kuczynski: Arch. f. Protistenkunde, 1918, xxxviii, 376.

[3] Ibid.: Centralbl. f. allg. Path. u. path. Anat., 1918, xxix, 279.

The following table summarizes the reports of different investigators with reference to Rickettsia bodies in connection with disease.

Year	Investigator	Rickettsia bodies or organisms resembling them found in
1909	Ricketts	Bacilli in blood of guinea pigs and monkeys infected with blood from Rocky Mountain spotted fever cases. Also seen in blood of man, and in female tick (*Dermacentor occidentalis*) and in eggs of these ticks fed upon infected guinea pigs.
1910	Ricketts and Wilder	Studies in Mexico. Bacilli in blood of typhus patients. Also in dejecta and various organs of lice fed on typhus patients. Occasionally found in faeces and intestinal contents of normal lice.
1910	Gavin and Girard	Blood of patients in Mexico. Significance of bodies obscure.
1912	Doehle	Discovered intraleucocytal bodies in scarlatina cases.
	Preisich	Recognized same bodies in other diseases.
1913	Prowazek	Blood of 51 typhus cases in Belgrade. In examination of sections of organs of typhus cases, trachoma-like bodies observed in endothelial cells of heart, lung, liver, kidney. One infected louse contained coccoid bodies and diplococcus forms.
1913	Mueller	Blood of typhus fever cases. Inoculated mice and rabbit.
1914	Sergent, Foley, and Vialatte	Lice living only on the sick, never in lice living on healthy people, or recurrent fever patients, in Algeria. Found especially in bloody fluid of digestive tract of the lice. A number of such lice fed on healthy individuals and proportion of microbes seen became much larger. Could not cultivate microörganism on artificial media.
1914	Nicolle, Blanc, and Conseil	Tunis, in 5 per cent of lice collected in districts free from typhus for two years. Lice fed on typhus cases are constantly infectious on ninth and tenth day, not before the eighth. Organisms not detected in blood and organs of guinea pigs infected with typhus.
1914	Rabinowitsch	In 1908 discovered *Diplobacillus exanthematicus* as the causative agent of typhus. Organism found in blood of typhus patients.
1915	Proescher	Blood smears from nine typhus cases showed bodies in endothelial cells from blood-vessels. Very few seen in plasma and in polynuclear leucocytes. These bodies not found in normal blood or in blood from cases of measles, mumps, scarlet fever, cholera, relapsing fever.
1916	Dorendorf	Blood of typhus fever cases in Serbia examined, and organisms described by Prowazek discovered in all cases examined during febrile stage — found in plasma and in polymorphonuclear and mononuclear leucocytes.

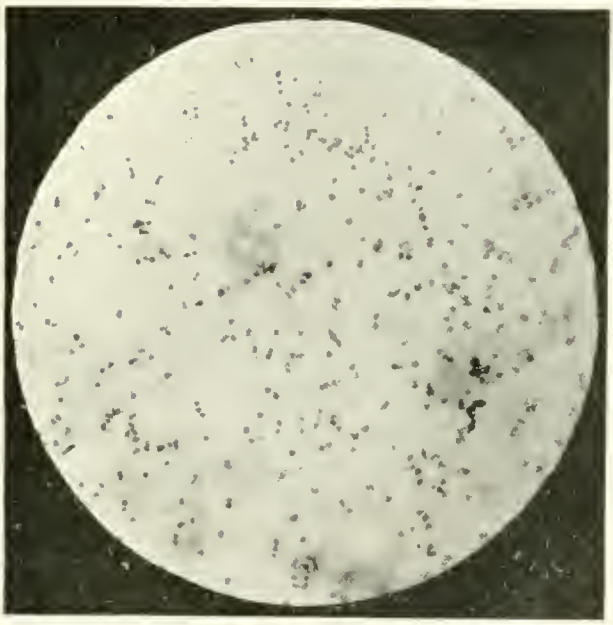
Year	Investigator	Rickettsia bodies or organisms resembling them found in
1916	Stempell	Among the enigmatic parasites in the intestinal epithelium in dissected lice collected from sick people.
1916	Lipschuetz	Polymorphonuclear leucocytes in blood from typhus cases; twenty-three examined, eighteen were positive. These bodies not found in control preparations from typhoid fever and variola cases, or in normal blood preparations.
1916	Csernel	Typhus blood.
1916	Zollenkopf	In describing a new disease resembling intermittent fever (probably Volhynia fever) found changes in red cells. Not found in preparations taken after the fever.
1916	Rocha-Lima and Prowazek	Investigations at Prison Camp, Kottbus, 95 per cent of lice taken from sick people were infected by parasitic microörganism. Organisms found in contents of alimentary canal, and especially in epithelial cells of alimentary tract. Not found in lice living on healthy subjects. Non-infected lice placed on sick patients became infected. This parasite found in man only in the leucocytes.
1916	Rocha-Lima	In 1914 (December) in streak preparations made from lice fed on typhus cases, found large numbers of bodies. Recognized by Prowazek as the same as seen by him in 1913 in preparation from infected louse. In examination of sections of lice from typhus cases, and of normal lice, bodies found in large numbers in cells of alimentary canal and in salivary glands of infected lice; not in normal lice. Seventeen out of eighteen lice from a sick patient were infected. Rickettsia appeared in cells of intestine of lice on fourth or fifth day. Louse fed on typhus patient showed Rickettsia four days afterwards.
1916	Wolbach	Bacillary bodies are present in large numbers in endothelial cells of guinea pigs infected with the virus of Rocky Mountain spotted fever through the bites of infected ticks.
1916	Wolbach	Organism found in experimentally infected ticks, similar to those previously seen in tissues of monkeys and guinea pigs, but never in non-infected ticks. Parasites most abundant in striped muscle, malpighian tubes, salivary glands, and ducts and brain ganglia. Numerous in muscle fibers of uterus and vagina, and seen in the spermatozoa. Also in lesions of blood-vessels in fatal human cases of Rocky Mountain spotted fever.
1916	Noeller	Lice from pigs transferred from infected guinea pigs to pig blood.

Year	Investigator	Rickettsia bodies or organisms resembling them found in
1916	Toepfer	Blood of Volhynia fever. Also in lice from typhus fever patients.
		Lice from typical Volhynia fever contained bodies in alimentary tract similar to typhus fever organism. Bodies both free and inside the cells.
1916	Toepfer	Examined smears and sections of 500 lice. Confirmed his former observations regarding organism in infected lice.
		Same parasite found in lice from heads of patients and in artificially infected normal lice of this species by placing them upon the sick. Smears from lice fed on typhus blood contained organism.
		Described intracellular diplobacilli in tissues of typhus patients.
1916	Hanser	Confirms Toepfer's discovery of forms in intestinal cells of lice fed on typhus patients.
1917	Munk and Rocha-Lima	Found diplobacillus in blood of Volhynia fever cases, but also found same in blood from patients with other diseases or even from healthy ones.
		Munk made 70 experiments on patients diagnosed as Volhynia fever cases, — 51 positive for *R. pediculi*, 11 negative, 6 doubtful. Among negatives were some typical cases.
		Among 33 control tests, 26 were negative and 6 infected same as lice from Volhynia fever cases. These 6 cases upon which the lice were fed which proved positive for Rickettsia were 3 malaria, 1 bladder disease, 1 bronchitis, 1 inguinal hernia. One normal gave rise to strongly infected lice.
		Rocha-Lima and Korbsch attempted propagation of Volhynia fever with lice, but not successful although lice were strongly infected.
1917	Toepfer and Schuessler	In 400 lice which had fed on 35 patients, bacteria-like organisms were found in the infected lice. Organisms found constantly in intestinal canal of lice removed from typhus patients and often in cells of alimentary tract. Control lice fed on other individuals than those suffering with typhus fever remained free. Organism found only in lice fed on blood of typhus patients during febrile (not post-febrile) period.
1917	Toepfer	In article on war nephritis describes similar organisms to those seen in lice fed on cases of typhus or Volhynia fever. Found similar organisms in 3 diseases, i. e., spotted fever, Volhynia fever, and nephritis.
1917	[Otto and Dietrich	In lice placed on patients. Infection not hereditary. They infected lice with Rickettsia by feeding them on a case of typhus fever without the exanthem.

Year	Investigator	Rickettsia bodies or organisms resembling them found in
1917	Lopez	Blood of typhus fever, found same intraleucocytal bodies, in 77 out of 90 cases. Blood must be taken from well-marked cases and at the height of the fever, to contain these bodies.
1917	Schmidt	Organisms found in 3 cases only, out of many cases of five-day fever examined.
1917	Jungmann and Kuczynski	Blood of typhus patients during first days of the rash, and also in trench fever. Had never found organism in other diseases.
1917	Werner and Benzler	In the stomach of lice fed upon cases of *febris quintana*.
1918	Brumpt	53 out of 72 body lice taken from healthy prisoners of war, pure culture found in the alimentary canal and in some cells. 16 lice from healthy prisoners of war were *all* infected, etc.
1918	Arkwright, Bacot, and Duncan	Lice fed on trench fever patients. Normal lice fed on persons not exposed to trench fever infection remained free from Rickettsia.
1918	Kuczynski	In the petechiae of typhus cases, in sections of liver in the endothelial cells of the capillaries, and in free phagocytic cells.

Our studies regarding the occurrence of Rickettsia bodies in lice which have fed upon healthy persons have confirmed those of a number of observers already referred to. Lice collected from healthy men in different parts of France, where neither typhus fever nor trench fever were present, were often found to contain Rickettsia in their dejecta: from 20 to 40 per cent of such lice examined, collected in different groups, revealing these bodies. In some of these normal lice, microscopical examination of the excreta or material from the alimentary tract showed them to be severely infected with Rickettsia bodies. Others were only moderately or very slightly infected, while in the remaining no definite Rickettsia were observed. Obviously from a microscopical examination, it is sometimes extremely difficult to say whether these bodies are not present in small numbers in the lice. Plate XXI, Figures 1 and 2, demonstrate the Rickettsia bodies in the excrement of *normal* lice.[1] There

[1] These photomicrographs were kindly made at the Pasteur Institute by Dr. P. Jeantet, who is in charge of the photomicrographic work of this Institute. I wish to express my thanks to both Dr. Roux, the Director of the Pasteur Institute, and to Dr. Jeantet, for this courtesy.



FIGS. 1 AND 2. RICKETTSIA BODIES IN THE EXCREMENT OF NORMAL LICE

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PLATE XXI

was not opportunity to search for them in the intestinal epithelium. The lice are referred to as normal because they produced no disease either in their original host from which they were collected, or when they were placed upon or fed upon other healthy individuals.

A critical examination of the literature regarding the relation of Rickettsia to disease reveals the fact that these bodies have been found in lice which have fed upon cases of typhus fever, Volhynia fever, trench fever, war nephritis, malaria, bronchitis, inflammation of the bladder, and inguinal hernia, as well as in a large number of lice collected in different parts of the world which have fed only on healthy people in whom they produced no disease. Rocha-Lima maintains that in lice, *Rickettsia prowazeki,* which is regarded by him as the probable cause of typhus fever, differs from *Rickettsia pediculi* (which is found in lice not infected with the virus of typhus) in that the latter does not occur normally in the epithelium of the alimentary canal of the louse. However, Toepfer, Brumpt, and others have reported the presence of Rickettsia in the intestinal epithelial cells of lice fed upon healthy individuals or in those fed upon Volhynia fever cases, or cases of war nephritis. Rickettsia have also been found in ticks that have fed upon cases of Rocky Mountain spotted fever. They have in addition been observed in the blood of man in a number of diseases, for example, in typhus fever, in Rocky Mountain spotted fever, in Volhynia fever, and trench fever. Rocha-Lima also believes that he has seen in the blood of healthy persons similar bodies to those observed in the blood of Volhynia fever by other investigators, and described by them under the name of Rickettsia.

Further, when we come to consider the aetiological significance of Rickettsia in human disease, it is apparent from the evidence already presented in this article that not one of the three classical postulates regarded necessary for the proof of the aetiological factor of an infectious disease has yet been demonstrated for the Rickettsia. (1) They have not been found in every case of the disease they have been said to be the

cause of; moreover they have been found in connection with other diseases than the one it is maintained they give rise to. (2) They have not been isolated and grown in pure culture.[1] (3) The disease which they are said to be the cause of has not been produced by the inoculation of such culture.

It seems very probable that the Rickettsia bodies are microorganisms, but as they have been found in lice from patients with so many different diseases, as well as in lice from healthy individuals, obviously no specificity for them could be justly claimed without further investigation. It is true that Rocha-Lima, Toepfer, and Olitsky, Denzer and Husk report the production of typhus infection in animals by the inoculation of the contents of the alimentary tract of infected lice. In this connection Rocha-Lima claimed that the disease developed in the inoculated animal because the Rickettsia were present in the lice used for the injections, while on the other hand, Olitsky, Denzer, and Husk claim the disease developed because the Plotz bacillus was present in the lice used in the inoculation of the animals. Obviously we can draw no definite conclusions from these experiments save that the infecting agent visible or invisible was present in the lice. Nothing can be said from them regarding the definite nature of the infecting agent. Sergent, Foley, Vialatte, and Brumpt all pointed out that the Rickettsia might merely accompany the infectious agent.

Observations and experiments recently made in connection with trench fever may be of interest in the study of Rickettsia. In relation to the aetiology of trench fever, as has been the case in the history of most infectious diseases, a number of widely differing microörganisms have previously been described as its cause, but none of these claims have been substantiated, and although very extensive studies have been made by a large number of observers, it is still a question whether the organism causing trench fever has yet been definitely seen in man either with the microscope or the ultramicroscope. Our experiments

[1] Kuczynski (Med. Klin., 1920, xvi, pp. 706, 733, 759) has since reported to have cultivated *R. prowazeki* in blood plasma modified to resemble human tissue lymph in celloidin capsules in the abdominal cavity of guinea pigs. He has also claimed to have produced typhus infection in guinea pigs with such cultures.

carried on in relation to the aetiology of trench fever have since shown that the causative organism of this disease is under certain circumstances filterable and that it bears some resemblance in its behavior to the filterable virus of hog cholera.[1] Our work regarding the filterable qualities of the virus of trench fever has recently been confirmed by Major General Sir John Rose Bradford, Captain E. F. Bashford, and Captain J. A. Wilson.[2] The organism causing trench fever being so minute is obviously separated only with great difficulty from the surrounding structures in the media in which it occurs naturally. Thus, while we have demonstrated that the virus of trench fever is present in the plasma of the blood of trench fever cases, in the febrile stages of the disease it is frequently very difficult to separate it from the blood corpuscles themselves by repeated washings of these with saline solution.[3] Also in the alimentary canal of the louse fed upon trench fever cases and in infected louse excrement, the virus on account of its minute size must be closely intermingled with other cellular structures present.

We have also seen that in different examinations of lice fed only upon healthy individuals, the Rickettsia have been demonstrated in from 20 to 74 per cent of them. Knowing these facts let us suppose that lice already containing such saprophytic Rickettsia in variable number had been fed upon trench fever cases and had become infected with the virus of trench fever, and such lice (containing the Rickettsia which may in the meantime have multiplied or increased in number) were then placed upon healthy human beings whom they subsequently infected with trench fever, obviously then erroneous conclusions might be drawn that the Rickettsia were themselves the aetiological factor of trench fever. It is evident that great difficulty would be experienced in a separation of the virus of trench fever from such bodies under the circumstances described above. Probably only by successful filtration ex-

[1] Trench Fever: Report of Commission of American Red Cross Research Committee, Oxford University Press, 1918.

[2] Bradford, Bashford, and Wilson: Brit. Med. Jour., 1919, i, 127.

[3] Loc. cit.: Trench Fever Report, p. 27.

periments, such as we have performed with lice excrement in connection with trench fever, could the separation be accomplished.

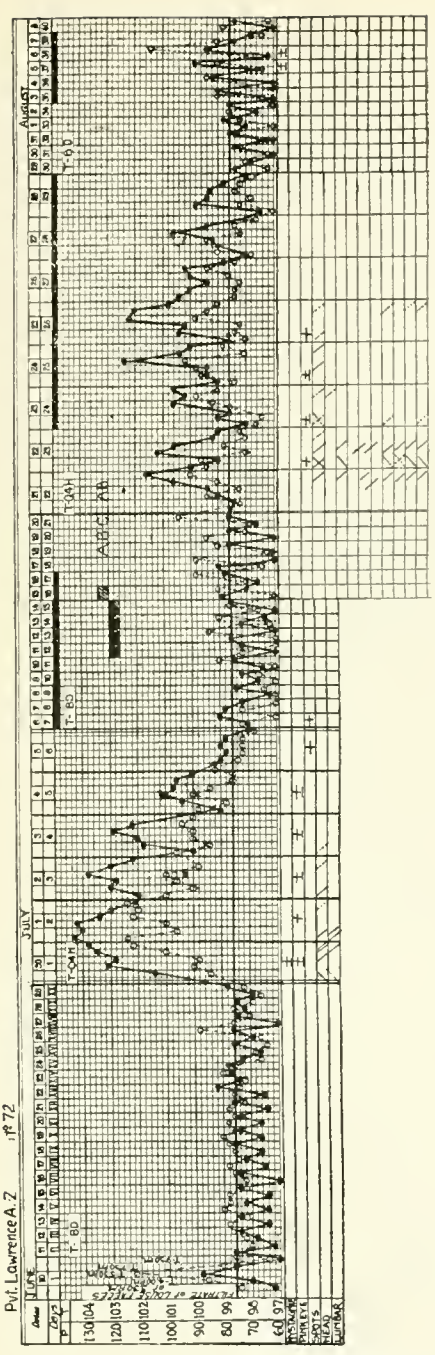
It of course may be argued that Rickettsia have a filterable stage as have other so-called chlamydozoa, and this idea receives some support from the fact that the virus of trench fever is under some circumstances filterable with difficulty, and attempts to infect human beings with the filtrates of infected material are often unsuccessful. Thus in ten filtration experiments performed with infected blood and urine from trench fever cases, and infected louse excrement, only three with urine gave undoubted positive results. The temperature charts of two cases of trench fever experimentally produced by the injection of the filtered trench fever virus are illustrated in Plate XXII.

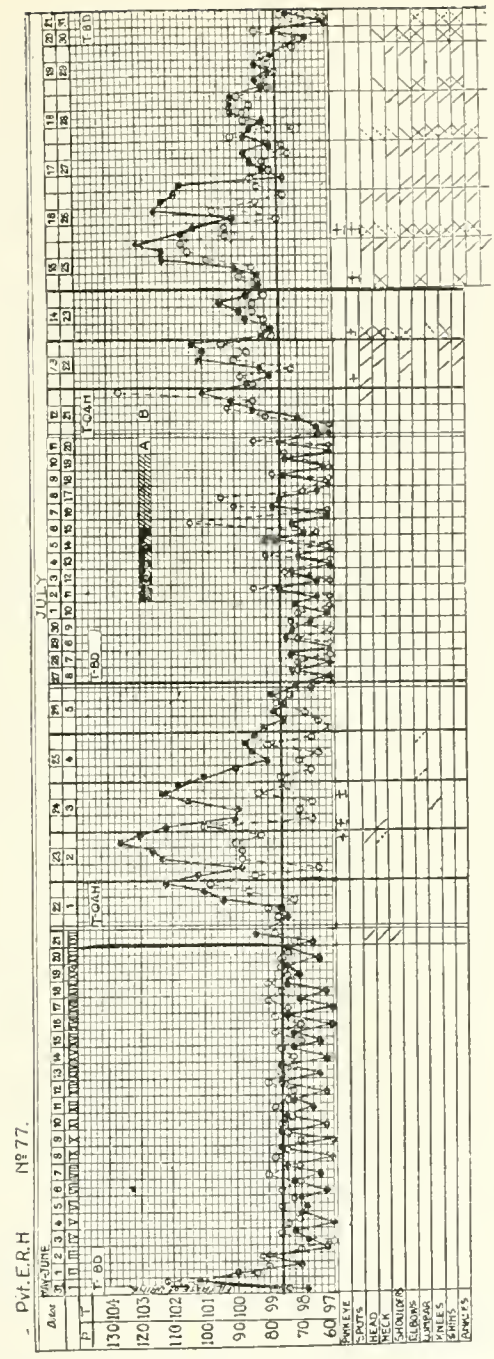
Bradford, Bashford, and Wilson [1] have since reported upon the cultivation of the trench fever virus from filtrates which have previously passed through porcelain filters and have also shown by human experiments that such filtrates contain the infectious agent.

It is conceivable that the Rickettsia, whether they possess a filterable stage or not, may be parasites of lice and not pathogenic for man, and Brumpt has suggested that the finding of them in human blood may simply be an indication that the individual has been previously infested with lice. On the other hand, there is the possibility that the bodies *sometimes* described as Rickettsia may constitute products of degenerated cells, for example, basophilic granules, which are more numerous in the blood in certain febrile diseases, in which case they would also increase in number in the lice fed upon such cases, and might then merely accompany the very minute or invisible aetiological factor of the disease. Finally, there may be at least three distinct species of Rickettsia, — *R. prowazeki*, *R. Volhynia*, and the third form either intra or extracellular, found in lice, and non-pathogenic for man.[2]

[1] Bradford, Bashford, and Wilson: loc. cit.

[2] Rocha-Lima: Deutsch. med. Wchnschr., 1919, p. 732.





FIGS. 1 AND 2. TEMPERATURE CHARTS OF TWO CASES OF EXPERIMENTALLY PRODUCED TRENCH FEVER

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PLATE XXII

In connection with the significance of Rickettsia as an aetiological factor in typhus, trench fever, and other diseases, it may be of interest to recall that in 1903 an organism described by Parker, Beyer, and Pothier as *Myxococcidium stegomyiae* was found in infected stegomyia mosquitoes, and was for a time supposed by these investigators to be the parasite causing yellow fever. Later this organism was found to be a species of yeast, and to occur not only in mosquitoes infected with the virus of yellow fever, but also in those not infected with such virus, and the virus of yellow fever was shown to be filterable and supposedly ultramicroscopic.[1]

From a review of the evidence presented in this paper regarding Rickettsia, it appeared obvious that until more definite results were obtained from further experimental work that we were not justified in finally concluding that the Rickettsia have a definite specific aetiological significance in relation to typhus fever, even though there was much evidence in favor of this idea. Hence it seemed advisable for the Medical Department of the League of Red Cross Societies to appoint a special Commission to study anew the question of the aetiology of this disease. This Commission, consisting of Dr. S. B. Wolbach of Harvard University, chairman, and a staff of seven members including Dr. John L. Todd, associate professor of parasitology at McGill University, Dr. A. Bacot, entomologist of the Lister Institute, London, and Dr. Frank W. Palfrey, instructor in medicine at Harvard University, have now nearly completed their investigations upon the aetiology of this disease and their full report upon this subject will shortly be published.[2] Their very painstaking and careful studies seem to show that typhus fever is caused by the *Rickettsia prowazeki* of Rocha-Lima.

However, while there has been much difference of opinion [3] regarding the specific organism of typhus fever, as we are familiar with the method of transmission of the disease, the

[1] Noguchi's recent experiments, however, point to the fact that the organism of yellow fever is a spirochaete. This according to other experiments is filterable at least at one stage of its life history. (Jour. Am. Med. Assn., 1919, lxxii, 187.)

[2] Wolbach, Todd, and Palfrey: Intern. Jour. Pub. Health, Geneva, 1920, ii, 211.

[3] Nicolle: Bull. de l'Inst. Pasteur, 1920, xviii, 1.

exact nature of the aetiological factor in connection with the control of epidemics is of importance particularly in connection with the hope that when the organism causing the disease has been definitely isolated and cultivated, a satisfactory form of protective inoculation or a satisfactory method of serum-therapy will be developed.

Weil-Felix Reaction

The Weil-Felix reaction (agglutination or clumping of *Bacillus proteus X 19* obtained from the urine of cases of typhus by the serum of typhus fever cases in dilutions of 1–100 to 1–2000 or higher) was not described by Weil and Felix until 1916, although Wilson [1] had isolated in 1910 from the faeces of one case and from the urine of two cases a variant form of *B. coli communis* which was agglutinated by the serum of seventeen cases of typhus and not by normal serum. Very extensive experiments performed since 1916 have demonstrated that the Weil-Felix reaction occurs in from 90–100 per cent of typhus cases, and sometimes in dilutions of the serum as high as 1–30,000, about 50 per cent of the cases giving the reaction by the fifth day and practically all by the tenth day of the disease. Even though it is the consensus of opinion that the reaction is not specific, and that *Bacillus proteus X 19* cannot be identified as the cause of the disease, its value as a method of diagnosis of typhus is generally acknowledged. However, the value of the reaction as a means of diagnosis in typhus fever had not been emphasized in 1915, and the reaction was not employed in Serbia in our laboratories for the diagnosis of the disease. During the severe period of the epidemic, the admissions into the hospitals were so high as to have precluded the use of any such method, the diagnosis from the clinical manifestations of the disease being the only method at all practical under the circumstances already described.

Bacteriological Studies in Serbia

The bacteriological studies that were carried on in Serbia during the epidemic did not confirm the fact that any one of

[1] Wilson: Jour. Hyg., Lond., 1910, x, 155.

the bacteria previously described as specific was in fact the aetiological factor in the disease. The investigations carried on by Zinsser, Sellards, and Hopkins, of the American Red Cross Sanitary Commission, did not confirm the fact that the *Bacillus typhi exanthematici* described by Plotz was the aetiological factor, and no other organism was isolated which was regarded as specific. These investigations are referred to in greater detail later in this Report.[1]

Reference has also been made to the work of Topley who also failed during the Serbian epidemic to isolate the *Bacillus typhi exanthematici* of Plotz, though it was sought for. Topley, however, reported the finding of a diplococcus which he regarded as specific, but this isolation was not confirmed by other investigators.

Penfold, 1916,[2] was also not able to isolate the *Bacillus typhi exanthematici* though he too isolated a coccus from four cases of the disease. Muriel Robertson [3] was unable to immunize monkeys against typhus infection with this coccus. On the other hand, Plotz's colleagues, Olitsky, Denzer, and Husk,[4] and Baehr,[5] Paneth,[6] and Popoff,[7] have all reported the isolation of this organism from cases of typhus. With so many contradictory reports, and particularly when one compares the results of Plotz and his colleagues with those obtained by Rocha-Lima, Toepfer, Schuessler, Noeller, Wolbach, Todd, and others in relation to Rickettsia, it seems obvious at least that further experimental work will be necessary before unanimity of opinion is secured.

Course of Serbian Epidemic

As has been stated, the epidemic increased steadily through January, February, March, and April, reaching its height for all of Serbia in April. By this time almost one in five of the

[1] Wolbach, Todd, and Palfrey also failed to isolate this organism in their recent work in Poland.

[2] Penfold: loc. cit.

[3] Robertson: Jour. Path. and Bacteriol., 1917, xxi, 173.

[4] Olitsky, Denzer, and Husk: Jour. Am. Med. Assn., 1916, lxvi, 1692.

[5] Baehr: Jour. Infect. Dis., 1917, xx, 201.

[6] Paneth: Med. Klin., 1916, p. 647, and Arch. f. Hyg., 1916, lxxxvi, 63.

[7] Popoff: Deutsch. Med. Wchnschr., 1916, xlii, 471.

Serbian people had contracted the disease.[1] Toward the end of April, however, the effort throughout the country to overcome the spread of the disease had generally become determined and united. The greatest credit is due to the Serbian medical officers and other officials and to the Serbian people themselves, for the heroic and determined manner in which in the midst of their sufferings this anti-typhus campaign once organized was pursued by them, practically all attention and effort in Serbia being centered upon the extermination of the disease.

At this period there were engaged in combating the epidemic in addition to the Serbian sanitarians, doctors, and other officials, detachments of physicians, sanitarians, and nurses from France, Great Britain, Russia, Belgium, Holland, and the United States.

The foreign personnel consisted particularly of Colonel Jaubert with 100 French physicians and sanitarians; Sir Ralph Paget with a number of hospital units from Great Britain under the individual direction of Lady Paget (with Dr. Maitland as chief physician), Dr. Elsie Inglis, Dr. Alice Hutchinson of the Scottish Women Hospitals, Mrs. Stobart, Dr. Barrie, Dr. Berry, and Captain Bennet, also a military sanitary mission under Colonel Hunter with whom were Major Stammers and Captain Topley with twenty-one lieutenants; a contingent of Russian, Belgian, and a few Dutch physicians employed in connection with the Serbian army; the American Red Cross hospital units under the general direction of Dr. Edward Ryan at Belgrade; the American Red Cross hospital units of Dr. Ernest Magruder and Dr. James Donnelly (both of whom gave up their lives during the epidemic), of Dr. Ethan Flagg Butler

[1] It has been suggested that the reduction of passenger travel from two trains to one on one of the railways extending from the north through Kraguevatz on March 16 had a decided effect upon the admission of typhus cases to the hospitals in this district. This is undoubtedly true since fewer patients were brought or came by train to these hospitals during this period. On resumption of travel, however, more cases were again sent to these hospitals and their records began to show an increased admission of typhus cases. During the period of partially interrupted train service many of the typhus cases were evacuated by ambulances to other hospitals in central and southern Serbia. It should be noted that by March 16 typhus was widely disseminated throughout Serbia and hence measures taken locally obviously could not and did not materially affect the course of the disease throughout the country, and particularly its course in the civil population.

and Dr. Kirby-Smith; as well as a number of American physicians assigned to the Serbian army in addition to the sanitary commission of the American Red Cross, numbering in all approximately 100 physicians. Of the American Sanitary Commission, Dr. Thomas W. Jackson was chief sanitary inspector; Dr. Hans Zinsser, bacteriologist; Dr. Aldo Castellani, consultant in tropical medicine and bacteriology; Dr. George C. Shattuck, clinician; Dr. A. Watson Sellards, chief of clinical laboratory; Dr. B. W. Caldwell, hospital administrator; Dr. F. B. Grinnell, sanitary inspector; Mr. Edward Stuart, sanitary engineer; Dr. Hopkins, assistant bacteriologist; and Mr. Arthur S. Ward, secretary.

I wish particularly to emphasize that it was the combined efforts of the Serbian medical and sanitary officers and other officials and of the Serbian people themselves, together with those of the personnel of the foreign detachments referred to, which soon began to show definite effects upon the course of the epidemic and from the beginning of May until August, when the epidemic was at an end, the decline of fever cases, not in any one locality alone but throughout the country, was continual. The accompanying chart which shows the curve of fever cases, typhus, relapsing, and typhoid, in the civilian population throughout the country for this period, strikingly illustrates this fact. Undoubtedly the approach of warm weather aided not only the officials concerned, but the people themselves in the success of the campaign, but no one who was concerned with this campaign can doubt the efficacy of sanitary measures in connection with the prevention of the spread of typhus fever. If no such anti-typhus campaign had been carried out, it is extremely probable that the disease would have diminished during the summer months only to reappear with greater intensity during the following winter, which is what has happened in Poland.[1]

[1] Typhus appeared in Poland in epidemic form particularly in 1916. Satisfactory preventive measures were not carried out, and the hope was expressed that the disease would disappear during the summer. However, the arrival of summer seemed to have little or no effect in stopping the epidemic, though the number of cases was somewhat decreased during the summer months. Each summer the same hope has been expressed, the epidemic continues to rage, now in its fourth year.

The work of these various foreign units in Serbia referred to above has been reported upon in various publications made by their respective directors and hence will not further be alluded to here.

ACKNOWLEDGMENTS

It is perhaps proper, however, in this report of the American Red Cross to say something regarding the American Sanitary Commission, and to quote from a preliminary report[1] made to the American Red Cross in 1915 upon this subject and not widely circulated. "The American Red Cross and Rockefeller Foundation have supported the American Red Cross Sanitary Commission in every way and have supplied it with all the necessary equipment and personnel. Every request which I made was granted. I cannot speak too highly of the personnel of the Commission, and I do not believe that a finer and more competent group of sanitarians and physicians were ever gotten together. Much of the success of the work in Serbia was due to their efforts.

"In this brief statement it is impossible to do justice to all, but the names of Dr. Thomas W. Jackson, chief sanitary inspector, whom I left in charge after my departure; Dr. Hans Zinsser, bacteriologist; Dr. Francis B. Grinnell, sanitary inspector; Dr. George C. Shattuck, clinician; Dr. A. Watson Sellards, who had charge of the clinical laboratory work; Dr. B. W. Caldwell, hospital administrator, and Dr. Aldo Castellani, consultant in tropical medicine and bacteriology, are deserving of the highest mention. All of these gentlemen with the exception of Dr. Castellani, who joined shortly afterwards, went to Serbia as members of the first commission. The name of Mr. Edward Stuart, the sanitary engineer of the Commission, also calls for special mention. His advice and work in connection with the many important sanitary problems in Serbia have been invaluable.

"Among the second group of men attached to the Commission, Colonel Gale, Doctors Mendelssohn and Gruver, Mr. Brink and others, and among the still later arrivals Dr. Harry

[1] American Red Cross Magazine, 1915, x, 346.

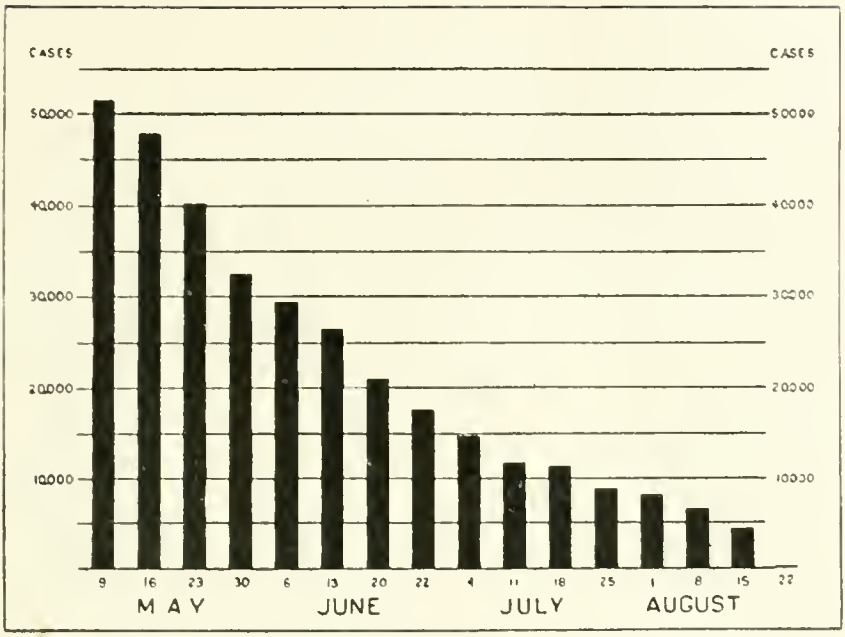

CHART SHOWING DECREASE IN FEVER CASES, TYPHUS, RELAPSING, AND TYPHOID AMONG THE CIVILIAN POPULATION, MAY TO AUGUST, 1915

PLATE XXIII

Forbes and Dr. J. G. Hopkins, all held responsible positions in the Serbian work."

Mr. Arthur S. Ward acted as secretary during the most trying periods of the epidemic, and Mr. Charles R. Cross, who afterwards died while performing other war service in France, was disbursing officer of the Commission, while Mr. D. B. Tripcevich and Mr. Ranko Jovanovich acted as interpreters and translators, particularly in connection with official records.

At the time of the organization in 1915 of the Commission, "Major General Gorgas, Surgeon General of the United States Army, most generously gave me his advice in relation to the equipment and personnel of this Commission, and I am glad to have this opportunity of expressing again my gratitude for this most valuable assistance. Later he generously offered to give up his position as head of the Medical Corps of the United States Army, if necessary, and come to Serbia if the epidemic could not be controlled. Fortunately for the army this sacrifice on his part did not become necessary.

"Surgeon General Rupert Blue, United States Public Health Service, and Colonel Fisher, Medical Corps, United States Army, have also made valuable recommendations, and Miss Boardman was untiring in her efforts of organization.

"Yale University, particularly through the offices of Professor Beebe, Madame Slavko Grouitch and others, and Harvard University, particularly through Dr. F. C. Shattuck and others, sent special funds for the work and Mrs. William H. Forbes, of Boston; Mrs. McMullen, of New Rochelle, and Mr. W. H. Converse have also generously given me financial assistance for relief work in Serbia.

"Through the International Sanitary Commission at Nish, the most complete and cordial coöperation was secured between the French, British, Russian, and American and other physicians and sanitarians working in Serbia. I cannot speak too highly of the work of many of my foreign colleagues. Among the British relief workers in Serbia the work of Lady Paget and of her husband, Sir Ralph, and of Sir Thomas Lipton, must be specifically mentioned. Lady Paget's hospital, which she

directed herself until she became a victim of typhus, and of which she again assumed the directorship as soon as she was convalescent, is equipped with over five hundred beds and has done most admirable work. It is only equalled in efficiency by one other hospital in Serbia. Sir Ralph Paget has worked untiringly and faithfully in the discharge of his duties, as has his wife. Sir Thomas Lipton,[1] apart from the financial support he has given and secured for Serbia, has encouraged and supported the medical and sanitary work in Serbia in many ways and has rendered innumerable kindnesses and supplied countless comforts for Red Cross workers in Serbia."

"The best equipped and managed hospital in Serbia is the American Hospital in Belgrade, of which Dr. Ryan is the director and Miss Gladwin the chief nurse. Here patients receive the same efficient care and comfort which they do in many of our best hospitals in the United States. Dr. Ryan, during the height of the epidemic, worn out with overwork, was stricken with typhus. He kept at work, however, until he became delirious, when he was taken charge of and treated by Dr. Kirby-Smith. As soon as his fever subsided, he resumed charge of his hospital. I could not do justice to the great work Dr. Ryan [2] has done in Serbia in a few words, and Miss Gladwin's work also merits the highest praise.

"Colonel Hunter and Major Stammers of the British Sanitary Unit also were of much assistance in the suppression of the epidemic, the former being in charge of the sanitary work of the army about Kraguevatz and the latter in charge of one of the sanitary vaccinating trains and other sanitary work for a part of the time. These gentlemen unfortunately were recalled to render aid to the British wounded in the Dardanelles. The French physicians, under the able leadership of Colonel Jaubert, and the Russian staff, under Colonel Solfatero, also rendered most important assistance.

[1] Sir Thomas Lipton on voyages with the *Erin* brought numerous physicians and nurses, and sixty tons of medicines and hospital comforts.

[2] Dr. Ryan and his assistant surgeons were in Belgrade during all of its bombardments and surrenders.

Sir Thomas Lipton on board the "Erin"

PLATE XXIV

Dr. Edward Ryan convalescing from typhus fever and
Miss Gladwin, chief nurse, A. R. C.

PLATE XXV

"Assistance that was particularly welcome was given by the American Relief Clearing House in Paris, especially through Messrs. Scott, Hargis, and Carter."

I wish to particularly express my appreciation to Miss Catherine M. Casassa, Secretary of the School of Tropical Medicine at Harvard University Medical School, for much valuable assistance in connection with the preparation of this entire Report, and for having read the proof of the same.

End of Epidemic

Writing in 1915 I expressed the opinion that the sanitary demonstrations and instruction in the prevention of typhus fever which had been given to the Serbian people, and the construction and use of the various permanent disinfesting plants which had been established through the country, would prevent the occurrence of another epidemic of such severity as to destroy in the neighborhood of 150,000 people.[1]

This opinion seems to have been justified and there has been no epidemic of this disease in Serbia of any magnitude since this time. However, typhus fever is and has been endemic in the Balkans for many years and a few cases of it still occur and others are introduced into Serbia from time to time.[2]

The Polish Epidemic of Typhus, 1916 . . .

On account of the assistance which the American Red Cross and other national Red Cross societies under the coördination of the League of Red Cross Societies are extending to Poland in connection with the typhus epidemic now raging in that country, it also seems advisable to review in this report the existing conditions in Poland, and the steps already taken in connection with this epidemic.

[1] The official record of the Secretary of War at Serbia gives the number of deaths from all cases for the army in 1915 as 171,725.

[2] Typhus fever was reported prevalent in Macedonia in 1919, the disease being traceable to refugees returning from Bulgaria, especially from Varna, and other Black Sea ports. A number of cases were reported present at Drama, but without spread of the disease. At Kavala about 300 cases were officially reported; the outbreak was successfully dealt with locally by Dr. Samuel J. Walker of the American Red Cross.

Russia as an Endemic Center of Typhus

Poland was formerly recognized as an endemic area of typhus and Russia itself has been regarded as one of the great endemic centers of typhus in Europe. Epidemics in Poland have occurred in the nineteenth century particularly in 1830–31, when the disease was introduced by troops, and in 1842–46 when there was a general epidemic throughout Poland. In Galicia where the disease is also regarded as endemic, we know that typhus was general in 1846–47; but complete statistics from these countries have not been available. However, for the ten years preceding 1916, in the whole of Russian Poland, with a population of about thirteen million, the average number of reported typhus fever cases was less than 2000 annually.[1] In all Congress Poland, before the war it has been estimated by the Polish Ministry of Health that there were in the neighborhood of 6000 cases annually. Low, 1916,[2] gives as the number of deaths from typhus fever for Galicia from 1895–1904 (ten years) 5592; and for 1905–12 (8 years only), 2181; while for Poland from 1905–11 (7 years), 1126.

The Present Polish Epidemic

Towards the latter part of 1916 typhus became epidemic in Poland, the chief area at first affected being the governmental district of Warsaw. This district at the time was occupied by German troops, and was then being administered as German territory. From the returns published by the Central Imperial Health Department in Berlin, it appeared that 26,099 cases were reported in about twelve months in the government district of Warsaw which had a population of only two and one-half million, 853,000 of which resided in the city of Warsaw. In Congress Poland and Galicia combined, the cases reported for 1916 were 34,538. The measures taken against the epidemic in 1916 and in 1917 failed to check its spread, but the hope was expressed that the epidemic would disappear in the summer months. The summer of 1917 however seemed to have little

[1] Lancet, London, 1918, i, 150.

[2] Low: Eleventh Annual Report, Local Government Board, 1914–15.

effect in reducing the number of cases of the disease, and for the year 1917 the cases for the same territory numbered 43,840. The epidemic was again not suspended the next year by the summer months, and in 1918 the number of cases more than doubled those in 1917, amounting to 97,082. Since December, 1918, Poland as an independent state has had control over this territory and the Polish government has carried on measures against the epidemic. During the first year of the existence of the Polish Public Health Service the number of cases of typhus reported to the Ministry of Public Health was as follows:

	Cases	Deaths	Per cent
Congress Poland	161,042	12,632	7.8
Galicia	70,158	7,250	10.3
Poznania	106	9	8.5
Total	231,306	19,891	8.6

During the months of January and February of 1920 the number of cases notified was as follows:

Congress Poland	12,098
Galicia	34,476

During the spring and summer of 1919 the disease showed a considerable decrease in certain portions of Congress Poland, but the number of cases again rose in November, and this number has remained practically stationary. Nevertheless it about equals the number of cases that were present during January and February a year ago (1919). In Galicia, however, the disease has not even remained stationary. There was a distinct rise in December, 1919, which has continued through January and February of 1920. These figures speak for themselves. They show that the epidemic is now well into its fourth year and they demonstrate that the measures which have been employed by the Polish government to combat the epidemic have not yet been as successful and as effective as was hoped. Colonel H. L. Gilchrist of the United States Army Medical Corps, attached to the Polish Ministry of Health, and fighting typhus fever in Poland, in a report written in March, 1920, says "the typhus epidemic which for the fourth year in succession has been raging in Poland, has increased in intensity

each year, due probably to the large influx of refugees and prisoners of war from Russia, and to the thousands of cases being imported from the interior of Ukrania and other eastern territories. The situation at present is getting beyond control."

In describing the conditions in parts of Galicia, he writes:

"In Galicia whole towns are crippled. Schools are closed and business practically suspended from the effects of the disease. In the northeast of Poland, American inspectors report the disease raging as affecting nearly every home, with a high mortality. Starvation and lack of clothing and medicines are also in evidence. There are few doctors and no nurses. As a result of the ravages of the past war, and the fact that Poland has been occupied by several armies which, when retreating, either destroyed or took with them all the materials of any value, the eastern country has been left with only absolutely meager essentials. Homes which for the most part are only rudely constructed affairs, and without furniture of any kind, offer shelter for thousands of these sufferers. They have no beds and lie on straw or hay-strewn floors. The same materials answer the purpose of protecting them against the Polish winters. Many of these small huts consist of but a single room, and here father, mother, and several children reside. The present article of diet in the majority of cases consists of potatoes, beets or other vegetables, and these in only starvation quantities. They seldom see bread. Meat is furnished only occasionally. At present nearly every house has from one to five cases of typhus fever, all lying on the usual beds of straw or hay. Houses have been visited by me in which the entire families were stricken, some delirious, and without medical attention of any kind. Some cases were found in which the only nourishment consisted of raw potatoes or raw beets. The friendly natives are doing what they can to relieve this suffering, but due to the shortage of the essentials of life their aid is of little avail. Doctors and nurses are unknown to these people, the peasants acting as combined doctors, nurses, and undertakers. If the dead have no near relatives to claim their effects, the bodies are stripped before burial and their clothing taken

away in ignorance by the peasants to distant parts to be sold, thus implanting the disease in new areas."

The circumstances which have been given by the Polish Minister of Health as responsible for the spread of the epidemic are:

1. The war devastation of Congress Poland and Galicia and its consequences.

2. The administrative chaos which followed the sudden withdrawal of the authorities occupying the Polish territories, and the disorderly demobilization as well as the reëmigration and the return movement of war prisoners from the East.

3. Great scarcity of sanitary materials and of professional personnel.

4. The absence of every kind of sanitary service in the eastern territories at the time of their occupation by the Polish troops.

5. The breaking up of the various Russian and Ukranian armies of Deniken, Petlura, Bredow, and the admission of these returning troops which the Polish government felt compelled to receive into their lines.

6. The impossibility of maintaining a rigid sanitary cordon on the eastern confines of the Polish civilian and military administration, owing to the lack of essential supplies and scarcity of personnel.

The Polish Minister of Health believes that the cause of the epidemic in Poland must be sought outside Polish borders and namely in the existence of a permanent focus of infection in Russia where according to Russian official sources 1,600,000 cases were notified during 1919. The Polish Minister reports that a campaign against the epidemic is being carried on particularly along the following lines: first, the establishment of a series of quarantine stations along the eastern borders of the country; through this line of stations it is stated that there passed between November 1, 1918, and January 1, 1920, 652,604 prisoners of war returning westward from Russia, and 627,088 reëmigrants flocking back to Poland from the East. Secondly, through the establishment of epidemic hospitals with a total of 13,077 beds and with a subsequent increase of some

7000 beds between September, 1919, and April 1, 1920. This number of beds does not, however, include those in the military hospitals at the front. Thirdly, by the establishment of mobile field sanitary columns 294 of which it is said they were operating in 1919, each employing a disinfecting apparatus. These columns carried out in the late summer and autumn of 1919 a mass cleaning-up campaign in the epidemic territory, and in all the counties of Poland. The Polish Minister states that "the number of people dealt with amounted to 311,374; 72,731 habitations were disinfected, and in addition to these, 19,400 people were bathed by four bathing motorized columns of Colonel Gilchrist's American Unit, while the units of the British Society of Friends have dealt with 15,860 people and 2800 habitations." In addition to these measures the report states railway stations on all Polish lines are being cleaned once weekly and the railway cars are being disinfected at three points. The erection of public bathing and delousing places is also being encouraged.

Action by the League of Red Cross Societies

Owing to the grave representations presented to the League of Red Cross Societies regarding the wide prevalence of typhus fever in Poland and the danger of its spread westward across Europe, it was decided that the League should interest itself in the control of this disease as an emergency relief measure. The importance of this step was particularly emphasized by the urgent request made to the League by the Polish Minister of Health for assistance in preventing the spread of the disease westward, and in the suppression of the epidemic in Poland itself.

At a conference held in Paris in June, 1919, at which the Minister of Public Health of Poland, then Dr. Janiszewski, Dr. Ludwik Rajchman, Mr. W. Frank Persons, Director of Department of Organization, League of Red Cross Societies, and the writer, were present, the Minister, in a written statement, requested that the League of Red Cross Societies should assist the Polish government in its campaign against typhus, and

presented two proposals in this connection: first, that the League of Red Cross Societies should take over the management of two lines of sanitary cordon (permanent and mobile) on the eastern frontier of Poland, organizing those stations which were not yet working; secondly, that the Ministry of Public Health should conduct a campaign on the territory of the late Congress Poland and Galicia, the Ministry applying to the Supreme Economic Council for the acquisition of necessary supplies; and that the League of Red Cross Societies should help the Ministry in obtaining the services of suitable salaried personnel. In the second proposal, the Minister stated, — "that I am most anxious to see a very close coöperation between the League and our own public health service, and this is the reason why I am bringing forward now a new proposition which we did not discuss at our meeting this afternoon, but which appears to me to secure that end better than the first scheme. It would consist in the following: (1) the Ministry to obtain supplies from the Economic Council as under the first alternative; (2) the Ministry would organize a Central Committee for fighting typhus in Poland. This Committee would appoint one delegate who conjointly with one delegate of the League of Red Cross Societies would conduct the whole action of combating typhus in Poland in accordance with the scheme of organization propounded in the annexed memorandum."

In connection with assisting the Polish Minister to obtain personnel, Colonel H. L. Gilchrist of the United States Army Medical Service, who had had wide experience in disinfesting troops, having been in command of such work in the American Expeditionary Forces in France subsequent to the Armistice, was invited to meet the Polish Minister of Health at one of these conferences with the idea of enlisting his services and those of his sanitary detachment in connection with the anti-typhus campaign in Poland. In a previous conference held with Mr. Herbert Hoover, American representative of the Supreme Economic Council, and representatives of the League of Red Cross Societies, it had been agreed that the Supreme Economic Council would interest itself in securing for Poland

necessary sanitary and medical supplies from the surplus stores of the United States Army, and that the League of Red Cross Societies would interest itself in attempting to obtain the medical and sanitary personnel desired by the Polish Minister. As the matter, however, seemed to be an urgent one, Mr. Hoover, at the same time that he arranged for the sale to the Polish government of these supplies, also presented to the President of the United States, at the time of his departure from France, the question of the detail of Colonel Gilchrist and his sanitary detachment for work in Poland, and this officer and his detachment were subsequently ordered by the Secretary of War of the United States for assignment to the Polish Minister of Health for duty. Unfortunately, it apparently was not recognized that the Polish Minister of Health did not have jurisdiction over much of the territory of Poland in which typhus was at its worst, such territory being under military authority; hence the services of this sanitary detachment were only available in Congress Poland where the Polish Minister of Health had jurisdiction.

The sanitary and hospital supplies purchased by Poland on credit at this time for the epidemic campaign from the American Liquidation Board alone were valued at a greatly reduced price at four million dollars. These supplies required thirty-two trains each of over fifty cars to transmit the material into Poland. Included in this equipment were the following important items: all the steam sterilizers which were not used by the American Forces in France; 27 mobile steam laundries; 500 mules with harnesses, hundreds of carts, drags, etc.; 10,000 beds; 40,000 sheets, blankets, and pillow slips; 40,000 towels; 100 tons of soap; 17 motorized bath plants; 300 portable bathing plants; 4000 Serbian barrels; 50 tons of washing soda; 1 million suits of cotton underclothing; 160 5-ton Packard trucks; 324 Ford ambulances; 160 Ford touring cars; 3 mobile machine shops, together with hundreds of other items too numerous to mention.

In order that the League of Red Cross Societies might be in a position to act most intelligently in connection with the re-

quests of the Polish Minister, the writer, as General Medical Director of the League, after consulting with the Chairman and other officers of the International Office of Public Health, and the officials of the British Ministry of Health, recommended that an Interallied Commission consisting of Assistant Surgeon General Hugh S. Cumming (now Surgeon General of the United States Public Health Service); Dr. George S. Buchanan, Senior Medical Officer, British Ministry of Health; Dr. Aldo Castellani, Lieutenant Colonel Italian Medical Service, and Dr. F. Visbecq, Médécin principal de première classe, French Army, Service de Santé, be appointed to proceed to Poland for the purpose of making a careful investigation of the medical and sanitary conditions in that country. This Commission, upon its return from Poland, rendered a comprehensive report to the League, summarizing the knowledge of medical and sanitary conditions in that country, and making recommendations of the measures which should be undertaken and the personnel and medical and sanitary supplies which should be furnished for the campaign against typhus fever and other infectious diseases epidemic there. It also pointed out that for the protection of Eastern Europe and of other regions, it is essential that the Polish government should receive help in the fight against typhus and other epidemic diseases, not only in Poland proper, but along the eastern frontiers through which infectious diseases are being constantly introduced by refugees and prisoners, and are liable to spread immediately into the interior of the country. On account of the magnitude of the task, the Director General of the League pointed out that the case seemed to be one which called for active assistance from governments as well as from voluntary organizations, and that it should be frankly stated and generally understood that the resources of the Red Cross were insufficient to provide all the assistance required by Eastern Europe in this great emergency. The Report of this Medical Commission was, therefore, presented not only to the national Red Cross societies, but also to the Secretary of the League of Nations and the Supreme Economic Council, with the request that all possible assistance be

given. A copy of this Report was also sent to the International Offices of Public Health at Paris. The Committee of this Office, after pointing out that it understands "that the League of Red Cross Societies considers the necessary action to be beyond what could be undertaken by the Red Cross organizations, and that the League has therefore presented the Report of its Commission to the various governments which are able to help by supplying material and personnel, and that it has insisted upon the necessity of the said governments helping in as great a measure as possible and as quickly as possible in the campaign against typhus in Poland which the Polish government is undertaking," states that the Committee of the International Office fully associates itself with the above suggestions, being convinced that the fight against typhus in Poland is of the utmost importance for the protection of other countries against the propagation of this terrible disease.

The League then took further action in connection with the Report of its Medical Commission and designated Mr. William C. Boyden as commissioner to Poland, and Colonel Henry A. Shaw as medical representative, who with a medical staff were sent to Poland to render such assistance as was possible for the League of Red Cross Societies to give the Polish government, and particularly to assist this government in carrying on an extensive campaign against typhus as had been requested by the Polish Minister of Health. The plan of campaign proposed included both field and sanitary work, comprising general disinfestation of people in badly infected districts, with removal of patients to infectious disease hospitals; disinfestation of other inmates and disinfection of the houses from which patients are taken; the establishment of quarantine and disinfesting stations, particularly in relation to the movement of refugees and the disinfection of railway trains and other vehicles of transportation; as well as the establishing, equipping, and running of hospitals for infectious diseases; the securing of personnel for the sanitary and hospital work, and provision for an educational campaign which would include the preparation of pamphlets and circulars upon infectious dis-

cases, printed in the language of the country, and practical demonstrations to be supplemented by cinematographic exhibitions on the public health measures concerned.

The League also arranged with Dr. S. Burt Wolbach of Harvard University and a staff of seven members, which included Dr. John L. Todd, associate professor of parasitology at McGill University, Dr. A. Bacot, entomologist of the Lister Institute, London, and Dr. Frank W. Palfrey, instructor in medicine at Harvard University, to make thorough investigations regarding the aetiology of typhus fever, particularly with the hope that new knowledge might eventually be obtained regarding its prevention by vaccination and its treatment by serum-therapy, and the report of this Commission has already been referred to.

Response to the Appeal of the League of Red Cross Societies

Following the appeal of the League for assistance in Poland from the national Red Cross societies, a generous response was obtained from the American, Australian, Belgian, British, Italian, Japanese, Portuguese, Roumanian, Serbian, and Spanish Red Cross societies. Also in the summer of 1919 the British government at the instance of the Supreme Economic Council contributed jointly with the British Red Cross, on a pound to pound basis, £60,000 for military and civilian relief work under the League of Red Cross Societies in Eastern Europe. Twenty thousand pounds of this amount were made available for Poland. The British Red Cross Society had already expended one hundred thousand pounds on hospital requirements, according to the Report on Economic Conditions in Central Europe, transmitted with Sir William Goode's despatch of January 1, 1920, and a further one hundred thousand pounds out of British credits was provided, which was to be used for the purchase of drugs and medical accessories.

The American Red Cross has been pursuing its activities in Poland under the direction of its commissioner, Lieutenant Colonel A. J. Chesley, since early in 1919. Its personnel at the present time in Poland, according to the statements of

Lieutenant Colonel Kendall Emerson, Deputy Commissioner to Europe of the American Red Cross, numbers 187. Since October 1, 1919, 378 carloads of supplies have been shipped to Poland. These include such articles as medical and hospital supplies, food, clothing, and motors for transportation. The relief work of the American Red Cross has included the general distribution of clothing to refugees, as well as medical care and advice; maintaining and operating delousing plants, and clinics and dispensaries; the equipping of hospitals and the establishment and operation of hospitals.

In addition the American Red Cross has heartly coöperated with the plans and activities of the League of Red Cross Societies relating to Poland and Eastern Europe, having donated $500,000 to the League to cover cost of investigations and surveys. It has also set aside $400,000 of its own funds for expenditure in Poland in accordance with the League's program.

Further Need of Personnel and Supplies

In a recent report made to the General Council of the League of Red Cross Societies by the writer, it was emphasized that further assistance is urgently needed, since typhus fever in certain districts of Poland is still on the increase, and the manner in which the national Red Cross societies can still be of particular assistance was reiterated as follows: in relation to personnel, it is suggested that physicians be furnished who should preferably have a special knowledge of infectious diseases and their treatment. These physicians would be stationed in the different hospitals for infectious diseases already established in Poland; other physicians should be bacteriologists with particular knowledge of public health laboratory work, while others should have special knowledge of field sanitation and should be preferably medical men trained as health officers or at least graduates of schools for health officers; sanitary engineers with special knowledge of water supplies and the sterilization of drinking water will also be required; nurses trained particularly for work in infectious diseases hospitals, and others trained for visiting and public health nursing are also greatly

needed. The writer has been informed by the Polish Minister of Health that *foreign units* rather than individual personnel of the nature described above are particularly desired.[1] Complete equipment for hospitals for infectious diseases is also urgently required.

The Interallied Medical Commission of the League sent to Poland also reported that the following supplies are indispensable for carrying on the campaign: soap, outer garments (for refugees and convalescents), linen, blankets, outer garments (particularly for patients), hospital equipment and mobile hospitals, drugs, various types of vehicles, delousing plants, both stationary and mobile; and particularly tools and material for construction of wooden buildings.

Importance of Further Administrative Measures in Combating the Epidemic

In a recent report made in March, 1920, Colonel Gilchrist writes: "After seven months of active work in Poland as the Commanding Officer of the American Typhus Fever Expedition . . . I am convinced that before typhus fever can be eliminated from Poland the entire matter will have to be placed under the control of a commission preferably international . . . which will have to have absolute control over all matters pertaining to the elimination of typhus fever in the country."

It has been pointed out that the Polish Minister of Health has not had jurisdiction over much of the territory in which typhus has particularly prevailed, such territory being under military administration, and that therefore there had not been as great coöperation and efficiency in prosecuting the campaign as was desirable. Recently, however, the Polish government has appointed Colonel Godlewski as Chief Epidemic Commissary, whose power it is said will extend over the whole of Poland including the country both under civil and military administration. Provided therefore that the Polish govern-

[1] The League of Red Cross Societies is at the present time about to issue a further appeal in connection with the relief of Poland.

ment will seriously impel and support the campaign there would seem to be every reason to feel that under the efficient direction of Colonel Godlewski, who has been placed in entire charge of this work, assisted by Colonel Shaw in charge of the inspection service, Colonel Gilchrist in charge of bathing and delousing work, and Colonel Chesley in charge of distribution of American supplies, we may look forward with confidence to the administration of the campaign. The present plan of campaign includes a comprehensive scheme for cleaning up central Poland inasmuch as all reports indicate that the disease has obtained a firm foothold throughout the entire territory of Poland and is no doubt spreading more or less extensively from these foci. It is the intention, however, that there should be no relaxation but an additional prosecution of the work of excluding the disease along the eastern and southern frontiers.

Poland, however, has so many serious problems confronting her that neither many of the governmental officials nor the people at large have as yet become thoroughly and sufficiently aroused to the importance and necessity of ridding the country of the disease. The epidemic has not been sufficiently prevalent or the mortality sufficiently high as to convince the people of the necessity for an intensive efficient anti-typhus campaign and of the inevitable inconveniences which must accompany it. Indeed the general attitude of many of the people in Poland is hostile to anti-typhus work, perhaps because often during the German occupation the people were compelled to submit to the necessary delousing measures which were applied by the Germans with military severity. As has been emphasized in this article in discussing the Serbian epidemic, one of the most important features in the suppression of this epidemic was the coöperation of the people in all efforts to eradicate the disease. In Serbia, however, the disease was general, and the very great majority of the families in the entire country has suffered from it. In Serbia also the mortality was in the neighborhood of 50 per cent, whereas in the Polish epidemic it has scarcely been above 9 per cent. As Colonel Shaw writes, it is manifestly impossible to compel a whole population to sub-

mit against their will to delousing measures. The first problem is to change their mental attitude so that they will be willing to coöperate and spread the doctrine of the campaign. For this reason it has been recommended that there should be instituted as an important part of the new campaign a comprehensive plan of education regarding the prevention of typhus designed to reach practically the entire population. Particular effort will be made to arouse and stimulate the activities of the people generally through religious organizations, schools, the press, through cinema exhibitions, relief organizations, magistrates, and other officials of towns and villages, and prominent business men. In this connection a play has been written by Major Richard Taylor of the staff of the League of Red Cross Societies, which is now being performed in Poland. This play, which is in the form of a drama, depicts the terror of this widespread disease, particularly among the poorer classes of the population in Poland, and at the same time it shows how it may be fought successfully by proper measures. One of the most interesting scenes depicts the arrival of a relief commission for health work in a village which is ravaged by typhus.

Dr. Buchanan of the Ministry of Health of Great Britain, and a member of the Interallied Medical Commission of the League of Red Cross Societies to Poland, since his return from Poland has not relaxed his efforts in Great Britain in connection with the medical relief of that country. Very recently at the British Ministry of Health an International Health Conference was held at the instigation of the Council of the League of Nations, at the sessions of which relating to Poland Dr. Buchanan presided. Representatives of the Polish government and of the League of Red Cross Societies furnished this Conference with information concerning Poland's needs in combating the typhus scourge; and the Conference agreed that action by the League of Nations was necessary. The measures necessary to combat this epidemic on a large scale were set forth, namely, the establishment of sanitary cordons, hospitals, delousing stations, the provision of food and fuel; and expert direction of the work; and it was recommended that, whenever

possible, surplus war materials be secured for use in Poland. The task of furnishing medical and sanitary personnel, nurses, and hospital units and certain supplies was to be carried on under the auspices of the League of Red Cross Societies. Resolutions relating to these activities were passed before the Conference adjourned. The League of Nations in connection with one of these resolutions has already appointed a Typhus Commission with Lieutenant Colonel Vaughan-Morgan as Chief Commissioner, and Dr. Norman White as Medical Commissioner. The League of Red Cross Societies will also be represented upon this Commission.

In view of this additional governmental assistance, we may then have greater hope that the epidemic will be soon brought under control.

Nevertheless, writing at this time, the writer feels it necessary to emphasize the fact that the anti-typhus campaign in Poland is even not yet being prosecuted by the Polish government in an energetic and satisfactory manner. While the greatest sympathy is due the Polish people and many of its officials for the terrible plight in which Poland has been placed by the war and on account of the several very grave war problems which she still has to face, all concerned in connection with this epidemic must nevertheless realize the fact that at no time during the past four years has the anti-typhus campaign been pursued with that activity and energy which is desirable and necessary to overcome the epidemic. Today the Polish government almost overwhelmed with military problems is less able than ever successfully to cope with the situation and foreign assistance seems imperative if this is to be accomplished. The government of Poland therefore not being in a position to deal successfully with the epidemic, an opportunity is obviously afforded to the League of Nations, in addition to the League of Red Cross Societies, to extend aid in this connection in that country. It should however be realized that the mere furnishing of supplies is not sufficient. If an additional large amount of sanitary equipment and vast hospital stores are sent to Poland without sufficient and efficient personnel to make proper use of

them, the effort in the light of past experience is liable to avail but little.[1] It therefore would seem to be exceedingly desirable that the League of Nations should extend its efforts not only to obtaining such material but should also particularly endeavor to arrange that a vigorous and really efficient anti-typhus campaign be waged and supported in every way practicable by the Polish government.

Typhus, however, is no longer a Polish question. It has become a world-wide question, demanding energetic measures. Besides the possibility of its spread to Western Europe and even by occasional cases across the Atlantic, and in addition to the industrial and social unrest which accompanies it, there is the fact that the economic rehabilitation of Eastern Europe cannot proceed satisfactorily until this disease is stamped out. Not only is it sapping the resources of Poland, it is causing other nations to set up barriers against her; it is fostering isolation in its most deadly form. For example, every person arriving in France from typhus-infected areas in Eastern Europe is liable to be subject to medical inspection and quarantine. In Great Britain regulations have been recently issued by the Ministry of Health extending and strengthening the powers of port and riparian sanitary authorities against the introduction of this disease. At Cherbourg and Rotterdam quarantine and disinfestation of all second and third class passengers coming from countries east of Switzerland and proceeding to the United States is already required. Nations are tightening, instead of relaxing, the cordon of their frontiers.

It is costing the world more to tolerate typhus than to eliminate it. It is a disease which spreads very rapidly and which is very deadly; but it is one which can be checked with sufficient men and material. The cost of "cleaning up" Poland would be less than the loss typhus now occasions.

If the world does not fight typhus in Poland, it may soon have to be fought not in those countries alone where it is liable to become epidemic but in others in which isolated cases of the disease will from time to time slip through quarantine and set up new centers of infection.

[1] See pages 99 and 100 of this Report.

PART II

CLINICAL OBSERVATIONS ON TYPHUS FEVER IN SERBIA IN 1915[1]

By GEORGE C. SHATTUCK

Prefatory Note

As clinical member of the American Red Cross Sanitary Commission it became my duty to study the clinical manifestations and treatment of typhus fever.

Near Skoplje or Uskub, occupying the buildings formerly used by the Military Academy, was situated the institution known as the Lady Paget Hospital, superintended by Lady Paget, with a staff of doctors of the British Red Cross in charge of Dr. Maitland. Before our arrival, early in May, this hospital had already become one of the principal fever hospitals of Serbia. It was proposed that Dr. Zinsser, our bacteriologist, Dr. Sellards, our clinical laboratory member, and I should pursue our investigations at the Lady Paget Hospital and we gladly availed ourselves of the opportunity.

The hospital consisted of two large three-story buildings devoted partly to wards and partly to quarters for the staff, and three pavilions, in each of which there were two large wards. One of these pavilions was put in my charge. Its wards accommodated ninety patients without overcrowding.

There were in May about four hundred patients in the hospital. New patients entered daily in variable numbers, generally a few at a time, but on one occasion eighty new patients arrived, and about forty of these were sent to my wards.

In the spring most of the patients in the hospital were suffering from typhus or its sequelae, but there were many cases of relapsing fever, a certain proportion of tuberculosis, and a small number of cases of other diseases. As the season advanced the proportion of typhus declined. Relapsing fever

[1] Prepared in 1916 as part of report of work done as a member of the American Red Cross Sanitary Commission to Serbia. Revised for publication April, 1920.

increased for a short time and then rapidly diminished, so that by the middle of July there were very few fresh cases of either disease in the hospital. Malaria was increasing rapidly, and dysentery of a mild form was becoming common. About this time I left the Paget Hospital at the request of Dr. Strong to take up other work.

Just before we began work Lady Paget and Dr. Maitland sailed for England, leaving Dr. E. Bellingham Smith in charge of the hospital. Through the courtesy of Dr. Smith, and of Dr. A. H. Holmes, another member of the staff, I was allowed to examine patients and to take notes in their wards.

The autopsies were performed by Dr. Zinsser, until he returned home in July, after which I performed a number of them.

The urinalyses were performed jointly by Dr. Sellards and me. Dr. Sellards made all the Sahli haemoglobin determinations, the red and white counts, most of the blood film examinations, and the Widal tests.

Dr. Dalyell, the British bacteriologist, kindly examined a number of blood films for the spirillum of relapsing fever, and was helpful in many ways.

To all of those mentioned and to the members of the British Staff in particular, it is a pleasure to express thanks.

Literature on Typhus

The distinguished men of medicine who have made important contributions to the knowledge of typhus, since it was clearly differentiated from typhoid by Gerhard, are too numerous to mention here.

The clinical descriptions of Gerhard,[1] William Jenner,[2] Murchison,[3] Curschmann,[4] Thoinot,[5] and Moore[6] are pre-

[1] Gerhard: Am. Jour. Med. Sc., 1837, xix, 289; xx, 289.

[2] Jenner: Med. Times and Gaz., Lond., 1849, xx, 401, 418, 456; xxi, 15, 113, 135, 233, 453.

[3] Murchison: Medico-Chir. Trans., Lond., 1850, xxxiii, 23. Continued Fevers of Great Britain, 3d ed., ed. by Cayley, Lond., 1884.

[4] Curschmann: Nothnagel's Encyc. of Pract. Med., Eng. trans., ed. by Osler, Phil. and Lond., 1901.

[5] Thoinot: Ann. d'Hyg., Par. 1915, 4th Series, xxiii, 6.

[6] Moore: Allbutt and Rolleston, System of Medicine, Lond., 1906, ii,

eminently good. Again, in the Gulstonian Lecture,[1] on the acute specific diseases, in which characteristics, resemblances, and differences are compared, Jenner's mastery of the subject is revealed. Stokes[2] recognized differences between typical typhoid and exanthematic typhus but, finding the "typhoid state" common to both, he believed to the last that they were varieties of the same disease. Nevertheless, his observations on circulatory conditions in these fevers are of great value.

The "Clinical Reports on Continued Fevers" comprising a careful analysis of 164 cases, by Austin Flint,[3] contain important observations on circulatory conditions and causes of death, and also an able summing up of the evidence then available for and against the view that typhus and typhoid fever are different diseases. He favored the conclusion that they were different but remained skeptical.

The pathology of typhus was first well described by Gerhard,[4] was discussed in detail by Murchison,[5] and summarized by Moore[6] and Thoinot.[7] Aschoff[8] and Prowazek[9] more recently studied it anew.

Important points for treatment were brought out by Gerhard,[10] Stokes,[11] Murchison,[12] and Castelloi (quoted by Doty[13]). Curschmann,[14] Moore,[15] and Doty[13] admirably discussed this aspect of the subject.

An extensive bibliography can be found in Murchison's book[16] and a list of the recent literature on typhus with ab-

[1] Jenner: Gulstonian Lectures, Lond., March, 1853.

[2] Stokes: Diseases of the Heart and Aorta, Lond., 1854; Lectures on Fever, Deliv. at Meath Hosp., Dublin, ed. in Phil., 1876.

[3] Flint: Clinical Reports on Continued Fever, Phil., 1855.

[4] Gerhard: loc. cit.

[5] Murchison: loc. cit.

[6] Moore: loc. cit.

[7] Thoinot: loc. cit.

[8] Aschoff: Med. Klin., 1915, ii, 798; Abst. Trop. Dis. Bull., 1916, vii, 148.

[9] Prowazek: Original, Beitr. z. Klin. d. Infections-krankheiten u. z. Immunitätsforschung, iv, No. 1; Med. Rec., N. Y., 1915, lxxxviii, 21. Editorial.

[10] Gerhard: loc. cit.

[11] Stokes: loc. cit.

[12] Murchison: loc. cit.

[13] Doty: Therapeusis of Internal Diseases, Forchheimer, N. Y., 1913, ii.

[14] Curschmann: loc. cit.

[15] Moore: loc. cit.

[16] Murchison: loc. cit.

stracts of many of the articles was published in the *Tropical Diseases Bulletin* [1] of March 15, 1916.

Many valuable articles have appeared recently about typhus epidemics in 1914 and 1915 and several are of unusual interest from the clinical standpoint. In this connection the following names require mention: Maitland,[2] Gastou,[3] Jurgens,[4] Michaud,[5] Milhit,[6] Siebert,[7] and Weiner.[8] Foster [9] described an epidemic in the Philippine Islands, Michie[10] published an account of his observations in Mexico, and Brill[11] has compared the endemic typhus of New York with the more virulent form seen in epidemics.

Usual Course of the Disease

An epitome of the typical course of typhus may be useful for comparison with the observations discussed later in this article.

The course of the disease has been divided into periods as follows: (1) *incubation;* (2) *invasion;* (3) *nervous excitement;* (4) *nervous depression;* (5) *defervescence;* (6) *convalescence.*

The duration of the incubation period or latent stage is given by different observers as from five to twenty-one days. According to Minkine it averages eight days; according to Netter, eleven; and according to Moore,[12] usually about twelve days. During this period there are no recognized symptoms.

The stage of invasion lasts from three to five days during which the temperature rises rapidly with slight morning remissions. The onset of symptoms is abrupt. A sense of extreme

[1] Bibliog. of recent work, typhus. Trop. Dis. Bull., 1916, vii, 137.
[2] Maitland: Brit. Med. Jour., 1915, p. 283.
[3] Gastou: Rev. de méd., 1915, xxxiv, 559.
[4] Jurgens: Zeitsch. f. ärzt. Fortbild., 1915, xii, 201; Berl. klin. Wchnschr., 1915, lii, 654.
[5] Michaud: Rev. méd. de la Suisse romande, 1914, xxxiv, 554.
[6] Milhit: Progrès méd., 3d Series, No. 32, 1915, p. 382.
[7] Siebert: Berl. Klin., 1916, xxvi, 1.
[8] Weiner: Wien. klin. Wchnschr., 1915, xxviii, 407.
[9] Foster: Arch. Int. Med., 1915, xvi, 363.
[10] Michie: Med. Rec., N. Y., 1915, lxxxvii, 214.
[11] Brill: ibid., lxxxviii, 914.
[12] Moore: loc. cit.

weakness often obliges the patient to remain in bed on the third day.

The stage of nervous excitement is characterized in severe cases by signs of acute toxaemia and by the development of the eruption which generally comes on the fourth or fifth day. This period lasts two or three days and is followed by the stage of nervous depression which is characterized by the "typhoid state." This condition does not develop, however, in mild or abortive cases.

Defervescence is generally rapid, but is very variable in duration and is accompanied, in favorable cases, by marked diminution in the symptoms of toxaemia. Failure to show such improvement when the temperature is falling in the usual way is universally regarded as a most unfavorable sign. It is at this stage or later that most of the deaths occur.

The duration of the fever was found by Murchison [1] to average between thirteen and fourteen days, in cases that recover. In his fatal cases it averaged fourteen to fifteen days.

Material and Plan of Work

Several hundred cases were observed and of these over 100 were studied in detail. Autopsies were performed in twenty cases. In three of these cases lesions of other diseases were found and the evidence of typhus is not absolutely certain. Many of the cases which came to autopsy were not under my care during life, and regarding these cases I have little or no clinical data.

Work was planned along the following lines: *firstly*, to observe the signs and symptoms with especial reference to diagnosis; *secondly*, to classify the varieties of the disease on the basis of prominent symptoms; and *thirdly*, to determine the cause of death as indicated by symptoms, autopsy findings, or both, with the object of improving treatment.

Case reports have been appended to illustrate the observations made. These cases have been grouped under the following heads:

[1] Murchison: loc. cit.

(*a*) Typhus with recovery — 13 cases.
(*b*) Typhus followed by death — with autopsy — 20 cases.
(*c*) Typhus followed by death — no autopsy — 2 cases.
(*d*) Diagnostic problems — 7 cases.

An index and list of numbers has been provided. It precedes the case reports. All case numbers mentioned in the text refer to the illustrative cases.

Observations

I. *Fever*

Of the onset there is little to say. In two mild cases which developed in the hospital the fever rose with moderate morning remissions, reached its maximum in four or five days, maintained a high level for a few days, and dropped by rapid lysis with marked morning remissions to normal again. In these cases the patient's strength returned quickly and convalescence was short.

Ordinary cases differed from these in greater severity of symptoms, more prolonged high fever, greater prostration, and slower return of strength.

Statements of the patients about duration of illness were not considered of much value because the patient was often too ill to given an intelligent answer, because it was difficult to ascertain whether he counted from the first symptoms or from the time when he took to his bed, and because the stage of the rash often indicated a probable duration which did not correspond with the patient's story.

The temperatures were all taken by rectum by the nurses and are, therefore, reliable.

Analysis of the charts shows that few patients were ill in the ward for more than four or five days before the temperature began to fall, showing that few were seen in the early stages.

The mean temperature before it began to fall varied in different cases from 102° to 105°; the greatest number having fever of 103.5° to 104°.

The daily fluctuations of the temperature during the period of high fever amounted, generally, to about one degree, and

seldom to more than two degrees. They were characterized by morning remissions and evening exacerbations, and this sequence was rarely disturbed.

The defervescence was nearly always by lysis with marked morning remissions. The duration of the lysis in different cases varied considerably.

Out of twenty charts in which the defervescence proceeded without interruption only two show the temperature dropping to normal within twelve hours. In four the lysis was rapid, lasting in two cases for two days, and in two other cases for three days. It lasted four days in five cases, five days in four cases, six days in three cases, seven days in one case, and eight days in one case. The proportion of cases with fever terminating by crisis in twelve hours was considerably smaller than these figures indicate. In fact, it was so unusual as to excite considerable interest.

It has usually been stated by the older authors that typhus fever terminates ordinarily by crisis, but many have since denied that this is the case. The dispute results largely from using the term *crisis* in different senses. To some of the older writers it signified a rapid improvement in the patient's condition, "a change so definite that one might name the day or even the hour when it began"; to others it signified a rapid fall of temperature as compared with the gradual descent in typhoid; and to this generation, more familiar with lobar pneumonia than with typhus, the word crisis has come to signify a precipitate drop of temperature from the original high level to normal or lower within less than twenty-four hours.

Two charts reproduced by Murchison[1] show gradual descent of the fever, and two others rapid descent, the shortest period of defervescence, however, being three days. That is to say, the fever in all these cases ended by lysis.

He says of the temperature: "After attaining its maximum there may be little change for several days, but some time between the seventh and tenth day, except in severe cases, there is usually a slight remission, and then the temperature gradually

[1] Murchison: loc. cit.

falls until about the fourteenth day, when it rapidly subsides to about the normal standard. In a single night it may fall from four to six degrees, but when there is pulmonary congestion, the fall is slower. Occasionally an elevation of two or more degrees precedes the final fall, and then a brief fall of moderate amount may intervene between the final rise and the rapid descent. This sudden fall of temperature about the fourteenth day is peculiar to typhus and may be useful in diagnosis. Before attaining its maximum the daily variations of temperature are slight, but during the second week they may amount to two degrees, the maximum being usually, but not always, in the evening."

Curschmann,[1] figures a series of charts which illustrate the points made by Murchison.[2] They show also great variations in the length of defervescence.

As compared with typhoid, typhus shows a marked tendency to rapid defervescence, but with lobar pneumonia as the standard, the reverse is true.

Murchison [2] says that a remission is to be expected about the seventh day; and Curschmann [3] observed remissions in some cases a few days before the beginning of the final defervescence.

None of my charts show this remission distinctly, but in some of them a secondary rise of temperature gives the appearance of an intercurrent relapse such as occurs in typhoid. Relapse is believed to occur in typhus fever extremely rarely, if at all. The secondary rises in my cases might be accounted for by complications.

Sweating, more or less profuse, was not infrequently associated with fall of temperature.

II. *The Skin*

The Eruption, according to Murchison,[4] generally appears on the fourth or fifth day.

In the few early cases that I saw, a scanty, pink, maculopapular rash was first discovered about the clavicles and on the

[1] Curschmann: loc. cit.
[2] Murchison: loc. cit.
[3] Curschmann: loc. cit.
[4] Murchison: loc. cit.

shoulders. On the succeeding day it was always widespread, and could be found more or less abundantly on the trunk, arms, legs, the backs of the hands and feet, and often on the palms and soles. It seemed to have no preference for flexor or extensor surfaces, it did not spread progressively, nor did it appear at intervals in crops, but it often became more abundant on the third day than it had been on the second.

Careful examination of the mouth and pharynx failed to show a definite eruption, but in a few cases several spots of doubtful significance were seen.

On the forehead near the edge of the hair, and on the scalp in several cases lesions were found which might either have belonged to the eruption or have been due to other causes. I saw not a single patient with a definite rash on the face, nor do I believe that any such occurred in the Lady Paget Hospital while I was there. Dr. Sellards, however, told me that he saw a pronounced eruption on the face in a fair-skinned patient in Belgrade, and that in this case the character of the lesions was the same on the face as on the body.

In the earliest stage the rash was rose pink, not dirty pink as described by some authors. Subsequently its color changed to red, then to purple in some cases and to rusty red in others. Before disappearing the remnants turned to a faded, dirty brown color. Most of the spots faded without leaving any pigment behind, whereas others, the darker ones, and especially those on the wrists, ankles, and backs of the hands, showed purple or brown haemorrhagic pigment, which persisted for a considerable number of days.

The remnants of the rash are rather characteristic but difficult to recognize with *certainty* when first seen at this stage, and particularly so when, as is often the case, the patient's body is sprinkled with minute ecchymoses resulting from flea bites. These ecchymoses differ as described below from typical typhus spots. Nevertheless, on the ground of this possible error, I have excluded from the list of undoubted typhus cases a considerable number that first came under observation at a late stage.

The change in color of the rash seems to be due to two causes: firstly, to increasing hyperaemia often followed by lividity, and secondly, to the deposit of brownish pigment. The amount of pigment was greater in the larger, elevated spots than in the smaller ones or in the macules. It seemed to be proportional to the degree of local congestion.

In the pink stage the color of the spots completely disappeared on pressure, in the red stage most of it disappeared leaving a faint rusty tinge, but in the cases in which the eruption became livid, pressure had little influence on the color of the lesions.

The spots did not all change color at the same time or in the same way. When the eruption was abundant, large pale pink, smaller rose pink, rusty red, and purple spots might be mixed together, and the predominance of one or another variety determined the general color.

"Subcuticular mottling" or "marbling" of the skin has been found by many observers associated with the spots and has been considered by them to be a part of the typhus eruption. It is clearly shown in the colored illustrations of Murchison,[1] Jenner,[2] and Curschmann.[3]

In a few of my cases vague, pale pink blotches were observed among the brighter spots at an early stage of the eruption, but they did not give a definite marble-like effect. In other instances the rash was so profuse that mottling could not have been readily distinguished if present. In the majority of the cases "subcuticular mottling" was looked for in vain, but in the case of Series No. 61, when the eruption was in an early stage and spots not very numerous, much pink mottling and blotches of irregular outline were observed, and in the case of Autopsy No. 25, a peculiar mottling was noted on the front of the chest during life.

Not infrequently, in the period of nervous depression, the limbs showed large, bluish, marble-like markings. They were associated with duskiness of the skin and resembled ordinary *cutis mormorata*. Probably they had nothing to do with the

[1] Murchison: loc. cit. [2] Jenner: loc. cit. [3] Curschmann: loc. cit.

eruption but should be regarded as local circulatory phenomena.

The typhus eruption is notoriously variable in appearance. The pictures of Jenner,[1] Murchison,[2] and Curschmann [3] show many differences in detail.

The eruption in our cases was so carefully examined that typical marbling could scarcely have been overlooked had it been visible when they arrived, but the dark skins of many of our patients may have rendered it invisible. Moreover, it seems probable that mottling or marbling is most distinct in the early stages of the eruption and may even disappear altogether after a few days. If this be so, failure to find it in more of our cases can be explained on the ground that most of them were not seen by us until the later stages indicated by the purple phase of the rash.

The spots of the eruption were macular or papular and were very slightly elevated. Generally, there were both macules and papules, the latter having irregular, ill-defined margins. Sometimes they were confluent, often they were very close together. When discrete they were roughly circular in shape. They varied in size from about one to three or four mm. in diameter. The variation was always considerable in the individual case, but in some patients the larger, and in others the smaller, lesions predominated. In profuse eruptions the larger type generally prevailed.

Dr. Smith showed me a patient in the early eruptive stage whose skin was almost as dark as that of the average negro. There was a profuse crop of small papular lesions clearly visible on account of their elevation but scarcely perceptible by their color. Papules were easily detected in many cases by palpation when the elevation was almost imperceptible to the eye.

Murchison [2] and Jenner [1] say that the rash is elevated only at first. This rule was not invariably true in my cases. On the contrary the larger and darker papules often remained elevated until the later stage when they had become haemorrhagic.

[1] Jenner: loc. cit. [2] Murchison: loc. cit. [3] Curschmann: loc. cit.

There seems to be a certain amount of confusion as to what is meant by the terms "petechial" and "mulberry rash."

Murchison [1] quotes Wilson [2] as follows: "When the sanguineous spots (of purpura) are minute they are termed *petechiae*," and it would seem, therefore, that this word should be used to signify *small haemorrhagic spots* like those of purpura. Keating's dictionary,[3] on the other hand, says under the head of petechiae: "It. *petechio*, 'flea bite.' *Small reddish spots on the skin like flea bites.*" Apparently the term has been used variously by different authors, but it is as good as any we have to describe the small haemorrhagic spots so common in typhus.

In typical cases the typhus eruption shows differences from purpura which should be emphasized. The spots of purpura are haemorrhagic from the beginning and sharply defined, whereas those of typhus are neither.

The fresh flea bite is distinguishable from the pink maculopapule of the early eruption by the haemorrhagic point in its center. The old flea bite differs from the petechial typhus macule in being of a brighter red color, more circular in shape, and in having a more sharply defined outline. Flea bites are more uniform in size, and are distributed chiefly on the body but typhus spots in the last stage generally show best on the wrists, ankles, and on the backs of hands or feet. Flea bites, however, may be so numerous on the body and limbs as strongly to suggest a typhus eruption and the fact that, in some cases, the typhus rash consists chiefly of small spots, leaves an opening for error. I saw two cases sent to the hospital with the diagnosis of typhus in which enormous numbers of flea bites were scattered all over the body and limbs. One of the patients probably did not have typhus, and in the other case, the diagnosis remained in doubt owing to the difficulty of distinguishing the eruption among the bites.

The term "mulberry rash" was first used by Jenner [4] who says that "the spots" . . . "have a dusky, pinkish-red color,

[1] Murchison: loc. cit.
[2] Wilson: Dis. of the Skin, 3d ed., 1851, p. 337.
[3] Keating: Dict. of Med., Phil., 1892.
[4] Jenner: loc. cit.

somewhat like the stains of mulberry juice." The term therefore serves to describe cases of profuse eruption in the later stages.

Hyperaemia. Coincident with the appearance of the rash, and perhaps earlier, there was a hyperaemic flush which was most pronounced over the malar prominences and on the ears. Later, the ears became bluish red, and the color in the malar region dull red. This coloring was peculiar and rather characteristic. It was considerably darker than the ordinary flush of fever, less sharply circumscribed, and less transitory. It often persisted well into the convalescent period.

Sometimes the hyperaemia extended mask-like across the nose and cheeks and up to the eyes, and a separate patch was seen over the end of the chin. In other cases, and particularly in the early stages of the rash, the entire face and neck were hyperaemic, and the redness often extended in a V-shape on to the upper part of the sternum. It showed a pronounced tendency to be limited to the parts which had been exposed to the sun, but in a few instances it was found also on the front of the chest and shoulders. In one case it covered the greater part of the trunk.

In the later stages of fever, the flush which had been due to active hyperaemia was replaced by congestion with cyanosis, or by a leaden hue, in those about to die. In other cases the malar flush persisted but the ears became cyanotic and the rest of the face assumed a muddy tint with underlying pallor.

Pigmentation. Repeatedly the face was observed to be decidedly browner in convalescence than it had been at the time of admission to the hospital. This was noted not only in those skins which had been darkened by exposure, but also in several patients having light complexions. It seems probable that the intense hyperaemia and prolonged congestion left behind some pigmentation analogous to that following exposure to the sun. The writer has found in the literature no mention of such an increase of pigmentation.

The *Taches Bleuâtres* were looked for but not found. Failure to find them may have been due to the rather dark skins of most

of our patients. Not only were their skins originally dark in most cases, but a multitude of bites and scratchings had added to the pigmentation.

When there was more or less acne intermingled with an eruption and a multitude of bites the picture was confusing.

Purpuric Spots were found singly in a few cases beneath the finger nails or on the pads of the fingers during convalescence. One of the latter developed into a small pustule.

Sudamina were frequently observed about the neck and shoulders.

Yellowness of the *palms* of the hands was noted in two cases late in the disease.

Herpes was observed repeatedly, most often on the ears, several times about the nose or lips, and occasionally on other parts of the face.

III. *Circulatory Signs and Symptoms*

Heart Rate and Pulse Rate. The pulse rate corresponded with that of the heart except when the pulse was extremely weak. In the case of Autopsy No. 23 on the last day of life such a discrepancy occurred.

In the first half of the febrile period the pulse rate was low, as a rule, in proportion to the temperature. It ranged most often between the upper eighties and one hundred or slightly higher with temperatures of 103° to 104°. Sometimes the pulse rate remained low throughout the illness (Series No. 48). In other cases, particularly in the sicker patients, the rate increased gradually to 120 (Series No. 59) or higher. Most of the patients whose pulse rate went above 130 died. Rates between 140 and 148 were counted, however, in a few patients who recovered (Series Nos. 9 and 93). The pulse often followed the temperature closely (Series Nos. 9, 61, and 93). In fatal cases with a terminal rise of temperature the pulse usually followed the temperature (Autopsy Nos. 18 and 25). Two patients dying with *moderate fever* had pulse rates that were *relatively high* (Autopsy Nos. 23 and 24) on the last days.

An old man who died suddenly and unexpectedly with a

temperature of 102.5° had a pulse rate of only 108. The autopsy showed a dilated heart with brownish, soft myocardium. The myocardial change was believed to be due in large measure to chronic degeneration (Autopsy No. 20).

With the decline of the fever, except in fatal cases, the pulse became slower. Frequently, after several days or a week of normal or subnormal temperature, there was a bradycardia with rates between 44 and 64, which lasted for three or four days. (Series Nos. 10 and 57.)

The bradycardia in Series No. 57 cannot be attributed to digitalis because the patient received none. In Series No. 10 digitalis was used, but was omitted two days before the pulse rate reached its lowest point. The digitalis may have caused it in this case. It almost certainly did so in the case of Series No. 83, in which heart-block seems to have developed.

Jenner [1] observed that the bradycardia following fever was brought about by lengthening of the diastolic pause and without change in the first sound, but that bradycardia due to cerebral conditions was characterized by a lengthened first sound and normal diastolic pause.

The disproportionate slowness of the pulse in relation to temperature, so common in typhoid fever, was not marked in my typhus cases. It was seen most often in the earlier stages of the illness. It seldom persisted until the beginning of defervescence.

Rhythm. With the exception of the supposed case of digitalis block mentioned under bradycardia, pronounced changes in the cardiac rhythm were not observed.

In most of the cases, however, in which the pulse became very weak it was found to be markedly irregular in force and slightly so in rhythm. A corresponding slight irregularity was noted in the heart's action.

Murchison [2] shows a series of sphygmographic tracings of the pulse after Sanderson. Murchison's Figure 6 corresponds to the bounding type of pulse. His Figure 7, which he calls "the irregular pulse of irritative fever," corresponds to that

[1] Jenner: loc. cit. [2] Murchison: loc. cit.

above described as being irregular in force and rhythm, and Figure 8, which he called the "irregular undulatory pulse of advanced typhus," depicts the small, weak or "thready" type of pulse. Measurement of this last tracing shows no variation in rate but slight differences in size of the waves. These variations seem to indicate fluctuations in pressure.

In his chapter on acute febrile affections of the heart (on p. 280, Figs. 169 and 170), Mackenzie [1] gives illustrative tracings of a type of irregularity which he attributed to failure of contractility. He says that he found this kind of arrhythmia in all his fatal cases of pneumonia. Murchison's [2] Figure 7 probably illustrates the same condition.

Mackenzie's [1] Figure 176, p. 286, shows a rapid pulse which is irregular in force but little, if at all, in rhythm. This type of pulse, he says, is "usually associated with greatly relaxed arteries, and a sphygmogram shows little or no sign of a dicrotic wave, indicating great lowering of the pressure during diastole of the heart." " Figures 172–176 show the characteristic features of the pulse in acute fatal pneumonia in a young, previously strong and healthy child."

Apparently, Mackenzie believed that the tracings on pp. 280 and 286 of his book represent varieties of arrhythmia due to the same cause, namely, to failure of contractility.

Hay [3] also figures an irregularity of force, without change in rhythm (Fig. 119, p. 158 of his book), which he says is found in "pneumonia, pericarditis, septic and other conditions, and indicates a grave prognosis."

The existence of irregularity in force of beats was strikingly demonstrated in the case of Series No. 10 on April 28 when, on taking the blood-pressure by auscultation under the cuff, some beats registered 90, others 70, and still others were not heard at all. (See also Series No. 9.)

Premature systoles were heard occasionally in Series No. 92.

Heart Sounds. The commonest abnormality was faintness, shortening, or blurring of the first sound. This was observed in

[1] Mackenzie: Diseases of the Heart, 3d ed., Lond., 1913. [2] Murchison: loc. cit.
[3] Hay: Graphic Methods in Heart Disease, Lond., 1909.

practically every case, and was generally the earliest change to develop and the last to disappear.

In most cases the second sound in the aortic area was diminished, but, at the same time, that at the apex might be accentuated. With the diminution in the second sound in the aortic area that in the pulmonic area became relatively louder. Sometimes it was definitely accentuated.

Normally loud, or even accentuated heart sounds sometimes accompanied a small weak pulse, suggesting that the circulatory deficiency was to be attributed to loss of tone of the vascular system rather than to weakness of the heart. (Autopsy No. 24, June 16.)

It has long been believed that vascular dilatation may cause circulatory weakness in typhoid fever. William Stokes [1] in 1854 devoted a chapter to the heart in "typhus fever." In the summary (par. 33) he says: "In certain cases of the worst maculated typhus an excited state of the heart may exist throughout the disease, although the pulse be feeble and the extremities cold." This points to vascular dilatation.

His observations on the heart in fever are careful and interesting, but lose some of their value from the fact that, although recognizing symptomatic differences between typhoid, typhus, and relapsing fevers, he believed them to be varieties of the same disease, and did not always make it clear of which he was speaking.

Stokes seems not to have appreciated the interrelation of cardiac action and vascular tone.

Ortner [2] made an important contribution to this subject in a study of typhoid fever in 1904. He states that "stronger" cardiac action may compensate for diminished vascular tone, and thus maintain the normal blood-pressure.

The case of Series No. 9 illustrates accentuated heart sounds and small weak pulse followed on the next day by heart sounds of poor quality and a weaker pulse. Prompt improvement after an infusion of salt solution in this case points to the conclusion

[1] Stokes: loc. cit.

[2] Ortner: Verhandl. d. Cong. f. inn. Med., 1904, xxi, 255.

that the vessels were mainly at fault, but a subsequent infusion brought out presumptive signs of cardiac weakness also.

In the case of Series No. 10 the heart sounds were never good while the patient was under observation, the pulse was always irregular in force, and heart dulness to the right became increased. When drugs failed to act salt solution was tried, but without much benefit. The second infusion was discontinued after a small quantity had been given because the heart failed to respond satisfactorily. In this case, whether or not there was vascular relaxation, the heart itself presumably was weak. These facts point to myocardial as well as to vascular disturbances and perhaps to diminution of contractility as suggested above.

Murmurs, systolic in time, were heard in many cases. Generally they were loudest in the pulmonic area and were not transmitted to the axilla. They were believed to be of functional origin.

Dilatation of the heart, evidenced by increase of dulness, was observed in the case of Series No. 10 only. At autopsy dilatation of the whole heart was found occasionally, but dilatation of the right ventricle alone was more common. In other cases there was no dilatation, and sometimes the heart was firmly contracted.

The Pulse was often of the bounding type particularly in the earlier part of the illness. Later it became small and softer. In the severer cases it was small and weak or "thready" when rapid. Occasionally, when it had been holding up well under digitalis, it would suddenly go to pieces, and the patient would seem to be in an alarming condition. After an injection of strychnin, of camphor, or of ether, however, it often improved promptly. This occurred once before anything had been administered, so that it is doubtful what would have happened in the other instances had nothing been done. Whether the phenomenon was of cardiac or vascular origin is uncertain. In the case of Autopsy No. 24 this condition recurred repeatedly.

There were other cases in which the pulse became weaker gradually, and several of these responded well to intravenous

saline infusions. Sometimes the infusion had to be repeated in from 12 to 24 hours. It was used most often when alarming weakness of the pulse persisted for some hours in spite of other stimulants. When there were signs of deficient ingestion of fluid, or after persistent diarrhoea, infusions were also used.

Pulses of poor quality often improved after the morning care and feeding, remained pretty satisfactory through the day, and weakened again in the evening. The nurses frequently reported cases in which death seemed imminent during the night although the condition during the day had been relatively good. They used hot drinks, strychnin, and camphor freely. I was often surprised in the morning to find patients still alive whose condition the evening before had been anything but encouraging.

In the case of Series No. 21, in which pulmonary symptoms were prominent, the pulse was notably good until and even after the death agony began. There was no autopsy.

Dicrotism, so common in typhoid fever, was looked for in all my cases, but was never found fully developed. Curschmann [1] says that it is rare in typhus.

Blood-pressure readings both systolic and diastolic were taken in most cases with the stethoscope below the cuff of the sphygmomanometer. The systolic pressure showed a tendency to fall gradually during the course of the disease. It was more or less reduced in practically every instance. It varied between the extreme limits of 75 and 125, but lay most often between 95 and 110 mm. of mercury. In convalescence it worked up again gradually.

The diastolic pressure level was generally between 65 and 75. The limits of difference were 30 and 85. Sometimes there was a marked reduction in diastolic pressure associated with a bounding pulse. (Series Nos. 1 and 49.) In the case of Series No. 49 the diastolic pressure soon rose again, but in Series Nos. 1 and 59 it remained low while the high fever lasted. More often the diastolic pressure was approximately proportional to the systolic pressure, i.e., equal to about three-quarters of it.

[1] Curschmann: loc. cit.

The case of Autopsy No. 24 showed a falling systolic and a *rising diastolic* pressure.

The pulse pressure in general showed a gradual fall until the beginning of convalescence. With the bounding type of pulse it was large. In the case of Series No. 59 it dropped from 80 to 50 with a drop in systolic pressure from 125 to 95. During this time the patient's condition was becoming progressively worse, but his pulse remained relatively good in volume. The reverse order took place in the case of Series No. 49. In this case, with a falling temperature and general improvement, the diastolic pressure rose from 50 to 70, and the systolic only from 105 to 110, so that again the pulse pressure was reduced. More commonly, in convalescence, the pulse pressure was increased by a gradual and marked rise in systolic and little change in the diastolic pressure. (Series No. 1.)

Several times in the later stages of the illness the Corrigan type of pulse was noted. In a case in which this was observed the blood-pressure was recorded at that time as 90 S–40 D. No diastolic murmur was heard. In the case referred to under Autopsy No. 5 with a similar pulse a diastolic murmur was heard, but at autopsy no lesion of the valve was found to explain it.

Such murmurs have been explained on the basis of failure of the aortic ring to contract, and a resulting relative insufficiency of the aortic value.

Ortner [1] reported such a condition in a case of typhoid fever.

Summary

Clinical evidence, therefore, points to the existence of myocardial as well as vascular disturbances in typhus.

A similar conclusion was reached by Ortner [1] in regard to typhoid fever.

Myocardial weakness appears to be decidedly more frequent, however, in typhus than in typhoid fever.

[1] Ortner: loc. cit.

IV. *Pathology of the Circulatory System*

The heart in our series of twenty autopsy cases presented a variety of conditions ranging from softness to firmness of the muscle, and from a state of general contraction to one of general dilatation of the chambers. The intermediate condition was represented by hearts in which the left ventricle was contracted and the right ventricle dilated or relaxed. Firmness of the muscle and contraction of the cavities generally went together, but in some of the contracted hearts the muscle was soft. It was soft, also, in all the dilated hearts, and in some of these it was pale in color.

Engorgement of the great vessels with blood was noted specifically in two cases in which the heart was soft, and in two in which it was contracted. Probably there was engorgement also in other cases in which it was not specifically noted. This engorgement seems not to have borne a definite relation either to softness or to dilatation of the heart.

Marked passive congestion of the lungs was found in eleven cases, but dilatation of the whole heart or of the right ventricle alone was observed in only six cases. In other words, passive congestion of the lungs bore no obvious relation to dilatation of the heart.

Of the cases with dilated hearts one died in the period of nervous depression, one during defervescence or later, and one in the postfebrile period.

Of the three cases with dilated right ventricles one died at the end of the period of nervous excitement, one in the postfebrile period, and one at an intermediate stage of the disease.

The two patients that showed merely relaxation of the right ventricle without dilatation died in the postfebrile period.

The cases permit of no deductions as to the frequency of cardiac dilatation in the stage of nervous excitement because there was only one death at that stage but, of the six cases above mentioned in which more or less dilatation was found, half of them died in the postfebrile period.

The relation of cardiac dilatation to symptoms may be worthy of investigation. In the case of Autopsy No. 5 there was slight dilatation and flabbiness of the muscle, but the pulse was relatively good until the day of the patient's death. The symptoms were those of cerebral toxaemia and exhaustion. In the case of Autopsy No. 12 the presenting symptom was coma associated with a soft and irregular pulse; and in the case referred to under Autopsy No. 22 weakness of the pulse was the only striking symptom for several days before death. There were no important complications in any of these cases. In the first of them the pulse gave no warning, by feebleness or irregularity, of weakness of the heart muscle. In the other two cases there was weakness and irregularity of the pulse.

The cases of Autopsy Nos. 6, 9, and 13 showed dilatation of the right ventricle. In that of No. 6 an old mitral stenosis was found. The violent delirium of No. 9 gave every reason to expect cardiac dilatation to develop even though the pulse was full and strong at first. In the case of No. 13 cardiac dilatation might have been inferred from the fact that the patient died in an attack of dyspnoea and distress.

The number of cases is too small to admit of safe deductions as to the relation of dilatation to symptoms. The same may be said of it as a possible factor in causing death.

The only other case in which either clinical or pathological evidence points to cardiac death is that of Autopsy No. 20. In this case there was weakness of the pulse and myocardial changes were found which seemed to be chronic, but the heart was not dilated. This patient died very suddenly.

If it be assumed that dilatation of the whole heart, or of the right ventricle, only found at autopsy, is evidence that cardiac weakness was an important cause of death in these cases and add to them the one last mentioned, it may be inferred that cardiac weakness was largely responsible for death in seven of the twenty cases autopsied.

But, if we subtract from these cases the one in which an old mitral stenosis of extreme degree was found, and the last case in which the myocardial changes seemed to be chronic, there

remain five cases in which acute myocardial weakness seems to have led to cardiac dilatation and death.

Three of these five, however, died in the postfebrile period in a state of emaciation and exhaustion from which they were unable to rally. Would it not be reasonable in these cases to suppose that death was due chiefly to general exhaustion rather than to the nature or degree of the changes in the heart muscle?

This view receives some support from the histological findings of Dr. Mallory. His studies of the pathological material, however, are not completed at the present writing, but sections have been examined from nine hearts selected to include some that were soft and dilated and others that were firmly contracted. Dr. Mallory says that slight fatty degeneration and small foci of cellular infiltration exist in all of these hearts to about the same degree, but that these changes are much less extensive than are usual in cases of diphtheria.

The evidence at hand seems to show that acute myocardial damage is seldom the most important factor in death from typhus.

Nevertheless, circulatory phenomena such as cyanosis, lividity, coldness of the extremities, and a pulse which is small, soft, and unequal or irregular are so common in typhus cases and develop so often a number of days before death, and low blood-pressure, small pulse pressure, and modification in the heart sounds are so constant in the severe cases of typhus that it *seems impossible to escape the conviction that circulatory abnormalities are of great importance and that they are a frequent immediate or contributory cause of death.*

The two italicized conclusions are reconcilable if the circulatory abnormalities be attributed less to myocardial lesions than to loss of vascular tone associated with dilatation of the vessels. Lesions in the walls of the blood-vessels, or the direct effect of toxins upon them, or the indirect influence of exhaustion, or perhaps a combination of influences acting on the vasomotor mechanism might bring about the dilatation.

Following this hypothesis deaths occurring before the period of defervescence may be attributed to toxaemia with resulting disturb-

ances of the vascular circulation; and later deaths could be explained as due primarily to general exhaustion and secondarily to vascular lesions or functional circulatory derangements.

My clinical observations accord well with this hypothesis, and, therefore, exhaustion was assigned as the principal cause of death in six of the seven cases in which death occurred in the postfebrile period. In the seventh case death was due to severe secondary infection.

In the cases that died earlier the toxaemia affected different systems in varying degrees. The case of Series No. 87, in which there was no autopsy, showed cerebral, pulmonary, and circulatory disturbances in a high degree. This case seems to be an instance of severe general toxaemia with incidental circulatory derangement. For two days before death weakness and rapidity of the pulse was the most alarming sign. In the case of Autopsy No. 24, on the other hand, exhaustion was followed late in the disease by circulatory weakness, and in that of Autopsy No. 9 cerebral toxaemia causing violent delirium was followed early by physical exhaustion, the pulse having been good during the period of delirious activity.

The first part of the aorta, in a large proportion of cases, showed a few small, soft, yellowish spots. Whether or not they developed in the course of the typhus or were there before it began is doubtful.

Murchison [1] says: — "In a large number of cases, the muscular tissue of the heart is flabby, soft, and easily torn." . . . "The softening is independent of the duration of the disease, the age of the patient, the external temperature, or the interval since death. In many cases it is confined to the *left side* of the heart."

Curschmann,[2] on the other hand, says: — "There is *almost always unilateral dilatation* of the *heart. In cases where death occurs relatively early,* the *muscle is flabby, friable, dull,* and of a *yellowish red color,* with occasional reddish streaks and linear and punctate markings. We unquestionably have to deal with the form of infectious myocarditis that has recently been

[1] Murchison: loc. cit. [2] Curschmann: loc. cit.

studied by the aid of modern microscopic technic in typhoid fever, scarlet fever, diphtheria, etc."

The histological changes, according to Moore,[1] are cloudy swelling and granular, fatty degeneration in the heart muscle. *Hyaline degeneration and necrosis of the inner coats of the small vessels in the skin* were observed by Prowazek.

The fact that in ten out of twenty of our autopsy cases the heart was found contracted and that the muscle of the *left ventricle* was soft in only two of these cases is of interest in relation to Murchison's [2] experience. In one of our cases the right ventricle was dilated and in two it was relaxed. Autopsy No. 9, the only case in which death occurred relatively early, showed softness of the muscle and dilatation of the right ventricle such as Curschmann's [3] statement would lead one to expect.

The theory which regards circulatory disturbances of vascular origin as an important cause of death receives some support from the findings of Prowazek.[4]

Summary

Lesions have been found in both heart and vessels in typhus. Clinical signs point to weakness of the heart in some cases, and to vascular dilatation in others. Most often the symptoms point to a combination of cardiac weakness and vascular dilatation.

The observations of Stokes [5] and of Jenner [6] in typhus and other fevers, the clinical work of Curschmann [7] and of Ortner [8] in typhoid, Wiesel's [9] histological studies of the heart and blood-vessels in typhoid, and the experiments of Stejskal [10] and of Romberg's [11] pupils with toxic substances, and the study of the pathology of the heart in diphtheria by Councilman, Mallory,

[1] Moore: loc. cit.
[2] Murchison: loc. cit.
[3] Curschmann: loc. cit.
[4] Prowazek: loc. cit.
[5] Stokes: loc. cit.
[6] Jenner: loc. cit.
[7] Curschmann: loc. cit.
[8] Ortner: loc. cit.
[9] Wiesel: Prag. Ztschr. f. Heilk., 1905, xxvi, 107.
[10] Stejskal: Ztschr. f. klin. Med., 1902, xliv, 367; 1903, li, 129.
[11] Romberg: Deut. Arch. f. klin. Med., 1899, lxiv, 652.

and Pearce [1] are of special interest in connection with the problem.

Tests of the functional capacity of the vasomotor mechanism and of the heart muscle have recently been performed by Porter and Newburgh [2] in experimental pneumonia, and Means [3] has studied the respiratory mechanism in pneumonia. The work of these men is extremely significant, throwing further light, as it does, on the nature of these circulatory changes.

V. *Blood*

Counts of the red and white cells, differential counts, examination of blood smears, and Widal tests were performed by Dr. Sellards, and have been discussed by him in another paper.

Dr. Sellards also made haemoglobin determinations of blood from the ear with Sahli's instrument. In some instances the percentages found were far above normal.

My own estimations were made with the Tallquist scale which is not adapted for abnormally high concentrations. In some cases it was evident that the blood was darker in color than the 100 per cent shade of the scale, and, accordingly, the observation was recorded as 110 per cent or 100 per cent plus.

Determinations by both the Tallquist and Sahli methods have been recorded on the charts of the illustrative cases.

There were marked differences in the results of the two methods. In an extreme instance of this sort the Sahli reading was 135 per cent and the Tallquist reading 85 per cent on the same day. More often, high color of the blood was recognized by means of the Tallquist scale and recorded as 110 per cent or 100 per cent plus, but the Sahli estimations were doubtless

[1] Councilman, Mallory, and Pearce: "Diphth. pathology of incl. heart." Jour. Boston Soc. Med. Sc., 1900, v, 139.

[2] Porter and Newburgh: Am. Jour. Physiol., 1908, xxiii, 131; Boston Med. and Surg. Jour., 1908, clviii, 73; Am. Jour. Physiol., 1914, xxxv, 1; Am. Jour. Med. Sc., 1915, cxlix, 204; Jour. Exper. Med., 1915, xxii, 123; Am. Jour. Physiol., 1915, xxxvi, 418.

[3] Means, Newburgh, and Porter: Boston Med. and Surg. Jour., 1915, clxxiii, 742; ibid., 1916, clxxiv, 464.

more accurate. Discrepancies may be explained in part by the fact that estimates by the two methods were never made simultaneously and local circulatory changes may have occurred in the interval.

High haemoglobin percentages with more or less increase of the red count were obtained in the cases of Series Nos. 9 and 10. These were among a group of patients that had spent several days on the train before reaching the hospital. All of them were not only markedly emaciated, but they also presented a dried up appearance as if they had not received sufficient fluid. Their high red counts might, therefore, be accounted for on the basis of dehydration of the blood as a whole. The estimate of haemoglobin of 135 per cent above mentioned may have been due to similar causes.

Another possible explanation for high red counts combined with high haemoglobin is irregular distribution with local accumulation of red cells. The frequent occurrence of marked local hyperaemia, often associated with slight cyanosis of the ears, favors this hypothesis as the more probable in some cases, if not in all.

Authority for such an hypothesis is provided by Cabot,[1] Wood,[2] and Sahli.[3]

Increase of the color indices is not so easily explainable. The indices were 1.13 in No. 9, and 1.10 in No. 10, the cases cited above. In Series No. 47 with a *normal red count* the index was approximately 1.15. In Series Nos. 1 and 57, *although the red counts were slightly low*, the indices were still higher. They were respectively 1.75, and approximately 1.30.

In the days when bleeding was practised as a routine in fever it was observed that the blood of typhus patients was abnormally dark in color and slow to clot. Dark color and fluidity of the blood at autopsy has been commented upon repeatedly, and was observed also by us. The question suggests itself as to whether methaemoglobin is formed in typhus. The

[1] Cabot: Clin. Exam. of the Blood, N. Y., 1901, p. 75.
[2] Wood: Chem. and Mic. Diag., N. Y., 1909, p. 127.
[3] Sahli: Diag. Methods, Trans., Phil., 1905, p. 628.

studies of Peabody[1] with the pneumococcus suggests that this may be the case. If so, a high color index could be attributed to the presence of methaemoglobin.

Repeated haemoglobin estimations by the Tallquist scale indicated that a slight anaemia develops in the later stages of typhus. Pallor during convalescence lent support to this view, and Curschmann [2] states that diminution of red count and of haemoglobin is found at the height of the fever and during convalescence.

VI. *Respiratory Signs and Symptoms*

Epistaxis was observed several times at the height of the disease (Series No. 21). Slight bleeding during convalescence was evidently caused, in one instance, by picking the nose which was ulcerated from herpes. Murchison [3] says that epistaxis is rare in typhus. Certainly, it is not so commonly an early symptom as in typhoid.

Pharynx and Tonsils. Reddening of the pharynx, the pillars of the fauces, and the tonsils, with slight swelling of the latter, seems to be common in the earlier stages of typhus. Pronounced catarrh of the pharynx associated with accumulation of tenacious sticky mucus which clogs the patient's throat and which is difficult for him to expel is a later condition. Toward the end of the period of high fever dried mucus is often seen adhering to the pharynx and giving it a glazed appearance.

The Larynx was seriously affected in only one of my patients. He was very ill when I first saw him and could scarcely make a sound. Later, he developed peculiar sepulchral tones. The voice was husky throughout convalescence but the subsequent recovery was complete.

In several other cases slight hoarseness was observed. None had obstructing oedema. Oedema of the larynx is one of the recognized dangers in typhus fever.

Lungs. Signs varied from those of slight passive congestion

[1] Peabody: Jour. Exp. Med., 1913, xvii, 587; 1913, xviii, 1 and 7.
[2] Curschmann: loc. cit.
[3] Murchison: loc. cit.

of the bases to evidence of rapidly developing, generalized oedema. Bronchitis was slight or severe. Lobular and lobar pneumonia were observed. Pain in the chest, probably pleuritic, was not uncommon, but no perfectly characteristic friction rub was heard, and pleural effusion was neither diagnosed nor found at autopsy.

Bronchitis. Autopsy generally showed the bronchial mucosa slightly swollen, injected, and bathed in glairy, sticky, blood-stained mucus. In other cases the bronchial secretion was mucopurulent.

Bronchitic râles were found in almost every case sooner or later. They increased as the fever advanced. They were scattered bilaterally throughout the chest. The râles, as a rule, were of the coarse, moist type; but piping râles were heard frequently. When the bronchitis was pronounced, sonorous rhonchi and fine moist râles were often present. The rhonchi could be heard all over the chest, but especially in the upper part; and the fine râles were generally limited to the bases, indicating that passive congestion was superimposed upon the bronchitis.

Passive Congestion was not found clinically except in the severer cases, and in these it was obscured by the bronchitis. Good nursing, I think, kept it at a minimum. In fatal cases which came to autopsy, however, passive congestion was found nearly always, and sometimes it was extreme.

Pneumonia, as a complication, was diagnosed at first on the basis of rapid, shallow, and labored breathing associated with inspiratory extension of the nostrils, use of the accessory muscles of respiration, and rather indefinite signs of consolidation consisting of slight dulness and distant bronchial breathing. The autopsy findings in some of these cases, however, were not typical of pneumonia, so that this diagnosis was later made with more reserve. This subject is again discussed under "Complications."

Atelectasis of small portions of the lung was found in several autopsies and may have explained some of the signs attributed to pneumonia.

Respiration. Movement of the nostrils and rapid but easy breathing was sometimes observed when there was no passive congestion and little if any bronchitis. In such cases the rapid breathing has been attributed by most authors to the action of toxins. Dissociation between the rates of pulse and respiration in typhus has been observed by many. Methaemoglobinaemia, if present, may have been a factor, and the question of acidosis requires consideration.

In other cases in which the breathing was rapid and labored, extensive bronchitis, or congestion, or both seemed to be the essential factors in its production. Series Nos. 21 and 87 died, apparently, by gradual drowning: which seems also to happen in some cases of pneumonia. There was no autopsy in either of these cases so that pneumonia cannot be excluded. Extensive pulmonary oedema existed undoubtedly in both cases. These patients were obliged to struggle for breath for several days before death, without rest or sleep.

The Sputum in cases of this sort was extremely viscid and could be expelled by the patient only with the greatest difficulty. It was often blood streaked. In other cases with manifest bronchitis it was mucopurulent or purulent.

Pulmonary symptoms were far more prominent in my typhus patients than they commonly are in typhoid or in any other disease with which I am familiar, except pneumonia. Pneumonia as a complication is discussed below.

Cough was a constant symptom. In many cases it was distressing not only by its frequency but also because of the effort required to expel the sticky secretion. Sometimes the patient almost choked in the process.

The Sputum, as a rule, was mucoid, tenacious, sometimes frothy, and often tinged or streaked with blood. At first it was glairy, later whitish, yellowish, or mucopurulent. Occasionally it was purulent, but this was due, probably, to a well-marked complicating bronchitis. Microscopical examinations were made in three cases in which pulmonary complications existed.

For several days one of these patients lay propped up in bed, the accessory muscles brought actively into play, and the

breathing rapid and laborious. The sputum was abundant, mucopurulent, and contained influenza-like bacilli and *Micrococcus catarrhalis* in large numbers, as well as a few pneumococci and some large bacilli. Bronchopneumonia almost certainly existed in this case.

The sputum in the case of Series No. 93 consisted of very viscid, thick, whitish mucus, and contained few leucocytes. There were many pneumococci and various other bacteria, among them a few influenza-like bacilli and spirochaetae. At times the sputum was foul-smelling and purulent but never copious, and a secondary rise of temperature occurred when the pulmonary symptoms became most marked. Gangrene and bronchiectasis were considered, but inasmuch as the cough and expectoration cleared up later it was probably a case of bronchitis and bronchopneumonia with retained secretion.

A third patient (Series No. 59) undoubtedly had pulmonary gangrene. A large quantity of frothy, tenacious sputum which later became extremely offensive was brought up in fits of laborious, spasmodic coughing during convalescence. Signs of trouble were found at the right base and there was pain in this region. The sputum contained great numbers of influenza-like bacilli, a few pneumococci, and bacteria of other kinds. Recovery was slow.

Tubercle bacilli were looked for in these cases but none were found.

VII. *Pathology of the Respiratory System*

The more severe lesions found at autopsy are described below under "Complications and Sequelae."

Bronchitis with swelling and redness of the mucous membrane has been described by others and is probably present in most severe cases of typhus.

Passive congestion was found in most of our fatal cases, but not invariably. There was none in the case of Autopsy No. 21.

Series No. 21, in which there was no autopsy, certainly died from asphyxia preceded by gradually increasing bronchitis, and pulmonary oedema. Perhaps there was pneumonia as well. Just before death the pulse was remarkably full and strong.

This was due probably to the rise of blood-pressure which usually accompanies asphyxia.

Wiener found lobar, lobular, or "hypostatic" pneumonia in one-third of his 39 autopsies. He mentions finding petechial haemorrhages in the larynx and large bronchi. To these he attributed the bloody sputum of some cases.

Bronchitis and pulmonary congestion in typhus seem seldom to result in death unless there is marked circulatory disorder, severe general toxaemia, extreme exhaustion, or pneumonia as well. Series No. 21 was unique among our cases in this respect.

There seem to be several varieties of pulmonary congestion. Sometimes it is chiefly of the hypostatic or passive type. In other cases it is localized in circumscribed areas and is intensely haemorrhagic in character suggesting that lobar pneumonia was developing. In still other cases in which congestion was not localized, the secretion was so viscid as to point to inflammation rather than passive congestion as its cause. In these cases it seemed to result from an intense bronchitis. These three types of process were often so intermingled as to render interpretation of the findings difficult (see "Pulmonary Complications").

The findings of Means, Newburgh, and Porter [1] in experimental pneumonia may have counterparts in typhus. If so, disturbances of the respiratory mechanism may play an important part in producing serious symptoms or death in typhus, and perhaps, some of the circulatory disturbances are secondary to disorders of respiration.

Peabody's [2] discovery of methaemoglobin in the blood of severe cases of pneumonia suggests that it may be formed also in typhus, and that it may explain the existence of cyanosis or dusky discoloration of the face in some cases in which the condition of the lungs and general circulation do not seem to warrant the change in color.

VIII. *Digestive System: Signs and Symptoms*

The Tongue was always coated, white at first, becoming later brown, dry, and often cracked. This is the "parrot tongue" of

[1] Means, Newburgh, and Porter: loc. cit.

[2] Peabody: loc. cit.

typhus. During convalescence it turned red along the edges first.

Brown Sordes accumulated with great rapidity on the teeth, so much so that in very sick patients it was practically impossible for the nurses to keep the mouth clean for an hour.

Anorexia was marked, as a rule, while the fever remained high, but appetite often began to return early in defervescence, and was generally good before the end of the febrile period. Many patients at this stage would sit up in bed and beg for more black bread when they were already receiving the usual amount and much other nourishment.

Vomiting of greenish bile occurred in a few cases. It was persistent only in one case (Series No. 57). No special cause was found for the symptom.

Haematemesis was observed once. It did not recur, nor was it followed by other gastric symptoms.

Abdomen. Pain was seldom complained of, but slight generalized sensitiveness to firm pressure was common. Gerhard [1] says that abdominal sensitiveness in typhus is usually a manifestation of a general hyperalgesia of the muscles or skin. This was true in some of my cases, but, as a rule, I think the sensitiveness was local.

The abdomen, generally, was flat or concave and quite unlike the doughy, slightly distended abdomen of typhoid.

Meteorism was unusual. It occurred in a few of the sicker patients who recovered and in a number of fatal cases (Series No. 87, death but no autopsy).

Pain and swelling in the lower abdomen resulting from overdistention of the bladder was seen in several cases (Series No. 9 and Autopsy No. 24).

Gurgling in the right iliac fossa was noted in two cases. Murchison [2] says that it is quite exceptional in typhus, and that when it does occur it is not limited to the right iliac fossa, and that it is associated with diarrhoea. One of my cases does not bear out this statement, for this patient had no diarrhoea. However, the gurgling may have been due to the transitory

[1] Gerhard: loc. cit. [2] Murchison: loc. cit.

effect of a cathartic. In Series No. 57 the gurgling was most marked in the right iliac fossa, but was not limited to that region. Here, again, there was no diarrhoea.

The Stools that I saw were dark colored, fluid, and rather uniform in appearance. A nurse told me that they were always liquid, but this may have been due to free use of cathartics, for Murchison [1] says that when the bowels move spontaneously without medicine the stools are usually of normal consistency and color.

Diarrhoea was pronounced in a few cases and slight in others. It began most often with the first indications of defervescence and lasted, as a rule, only two or three days. Series No. 59 had exceptional looseness of the bowels. The day before the crisis when his condition was desperate, they moved seven times. The diarrhoea continued for a considerable number of days and required opium to control it. A patient of Dr. Smith's that I did not think could live another day developed a severe diarrhoea coincident with the beginning of convalescence. Several fatal cases also had diarrhoea (Autopsy No. 24), and it was troublesome in Series No. 93.

The Spleen was felt in a small proportion of cases only. In a larger proportion there was increase of dulness in the splenic region. Adding together these two groups of cases and assuming that the increase of dulness was due to splenic enlargement, there was evidence of enlargement at the first examination in about half the cases. When not palpable at first the spleen was not felt later. Curschmann [2] says that the "enlargement rarely exceeds a moderate degree, and the consistence of the organ is, on the average, less than in other infectious diseases." He believes that the spleen can be felt, however, in most cases if examined early enough; that the enlargement comes with the first symptoms and that it generally disappears before the beginning of defervescence. Failure to feel the spleen may be accounted for in some cases probably by extreme softness of the organ, and in other cases because it may no longer be enlarged when the patient is first seen at a late stage of the disease.

[1] Murchison: loc. cit.

[2] Curschmann: loc. cit.

The Liver edge was felt in a few cases. There was never much enlargement.

In 1861 Barrallier [1] (quoted by Murchison [2]) found slight enlargement of the liver in 30.6 per cent of 365 cases.

Jaundice is not mentioned by Murchison [2] but Michie [3] found "slight haematogenous jaundice" in cases of Mexican typhus, and Michaud [4] saw five cases of jaundice associated with enlargement of the liver among fifty-eight cases of European typhus. He found urobilinuria in twenty-one cases of the same series. Wiener [5] says that he saw jaundice frequently in Hungary. Repeated tests for bile in high-colored urines from our cases were negative, nor was jaundice observed in any of them.

Intestinal Parasites. An ascaris was vomited up by several patients.

IX. *Pathology of the Digestive System*

Intestines. With the exception of a few minute ecchymoses found occasionally on the serous surfaces, and marked distention of the stomach, colon, or intestines in a few instances, nothing abnormal was observed.

Autopsy No. 26, however, in which endocarditis was found and the diagnosis of typhus uncertain, showed many minute red dots on the mucosa at the lower end of the ileum.

Wiener [5] says that haemorrhages in the submucosa of the colon can often be seen from without, that they are dark red, generally sharply circumscribed and paler at the edges. They varied much in size, and the extravasation sometimes extended all over the colon. Ecchymoses in or on the intestines have been described also by others.

Gastou [6] found the mucosa of the intestines and especially that of the colon congested, the folds prominent, and the walls thickened.

The Liver often showed nutmeg markings. Sometimes it was

[1] Barrallier: Du typhus épidémique à Toulon, Paris, 1861.
[2] Murchison: loc. cit.
[3] Michie: loc. cit.
[4] Michaud: loc. cit.
[5] Wiener: loc. cit.
[6] Gastou: loc. cit.

dark colored and engorged with blood. In other cases it seemed to show more or less fatty degeneration. Its size was normal or slightly increased.

The Spleen was generally enlarged, sometimes much enlarged and very soft. In a few cases it was firm and of normal size.

X. *The Nervous System: Signs and Symptoms*

Mental States. The facial expression varied between individuals and at different stages of the disease. It most often expressed stolid patience, indifference, or lethargy until toward the end of defervescence, when the patients began to ask for more food or to be allowed to go home. Those that were not very toxic were less somnolent than is the rule in typhoid. As the disease advanced the features became sharp and drawn.

In a group of about forty patients who entered my wards at about the same time, after having spent many hours, if not days, in transit, probably with little care, scanty food, and insufficient water, the expressions were strikingly alike. The face was pinched, the malar flush pronounced, the brows knitted immovably as if by pain long endured, and the eyes were watchful but showed no sign of emotion. The patients made no sound, nor moved at all in bed. They submitted passively to being examined, and although fully conscious, gave no sign of interest in what was being done.

Particularly in the days immediately preceding defervescence the mentality was clouded, and there was usually quiet delirium at night if not in the daytime. Many cases of this sort had carphology, subsultus, and intention tremor of the hands, and in some cases of severe toxaemia, twitching of the jaw and facial muscles was observed. Twitching of the arm muscles was brought on at times by passive motion of a limb or by taking the blood-pressure.

A Russian medical student (Series No. 87) who showed all of these symptoms retained enough understanding to grab for his chart when it was being examined before him. Later he became completely delirious, and died after a few days. Contrasting with this case was that of a Serbian officer (Series No.

21) who apparently appreciated his condition to the end. His nervous system showed little outward sign of intoxication.

Series No. 9 was somnolent on admission and later fell into a stupor but was never completely comatose. This case was complicated by nephritis, but the patient recovered. A fatal case of Dr. Holmes' (Autopsy No. 12) was in deep coma for about two days before death. The kidneys showed some abnormalities.

Stupor verging on coma was the rule in the sicker patients even in the absence of renal lesions, and few patients in which it was pronounced got well.

The typhoid state with fatal issue was well illustrated in the case of Autopsy No. 24.

Series No. 61 was troublesome by trying to leave the ward. He was not violent or excited except during one night when he had to be tied in bed.

Dr. Smith had a case of wild delirium analogous in all respects to delirium tremens. This patient slept only when exhausted. His pulse was very full and bounding at first, but he died apparently from pulmonary oedema or beginning pneumonia with cardiac dilatation.

A patient of mine (Autopsy No. 25) was somnolent but easily aroused. For days he refused food and medicine and drank scarcely any liquid. This condition persisted even when the temperature was down to normal.

Hyperemotionalism during the febrile period was illustrated by a man of middle age who was extremely thin and feeble when admitted. He begged tearfully to be sent home, and apparently expected to die, but he recovered. During convalescence normal control and cheerfulness returned quickly as a rule.

Early in defervescence nervous symptoms began to diminish and the appetite to return in favorable cases. When a change for the better was not coincident with a fall of temperature, the outlook was very unfavorable. Recovery of cheerfulness and mental activity was often astonishingly rapid, but in a few cases intellectual lethargy was persistent.

Marked intellectual debility and lack of control was seen in the case of a nurse returning home some weeks after typhus. Another nurse had hysterical tremor, emotionalism, and speech disturbance which persisted for weeks. In this case a perinephritic abscess was discovered and when it had been drained the symptoms passed off. Her attack of typhus had been mild. Hysteria was seen also in a man, a big Serbian, who was convalescent and doing well and who happened to have old suppurating glands of the neck. He developed tremor, lameness, and became very apprehensive after seeing a patient operated on for parotitis. He was relieved temporarily by the simplest suggestive methods but under like circumstances the symptoms recurred (Series No. 48).

Frontal headache was almost invariably complained of in the earlier stages of the fever. It lasted several days and did not return. Sometimes, also, there was pain in the eyes or at the nape of the neck.

Stiffness of the Neck and *Kernig's Sign* were found in a large number of cases. In a series of thirty-one cases the neck was stiff in all but three. The stiffness was slight in twenty-one cases and moderate or marked in seven cases.

Kernig's Sign in the same series was absent in three cases, present on one side only in one case, slight in twenty-three cases, and moderately developed in four cases. In one case the neck was moderately stiff but there was no Kernig's sign, in another there was a slight Kernig's sign but the neck was not stiff, and in two cases neither sign was found. The stiffness was due to muscular spasm, but could not be accounted for by sensitiveness of the muscles because this was much less common than spasm, and was often entirely absent in the presence of spasm. The spasm was seldom so pronounced as is usual in meningitis. It was attributed to meningeal irritation.

Stiffness of neck or legs was observed also in a few cases of disease which may have been mild typhus but which were not so considered. It was slight in these cases and in none of them was it considerable enough to be designated as "moderate" by comparison with that found in the typhus cases.

One patient (Autopsy No. 23) had pronounced twitching and tonic spasm of the arms as well as a very stiff neck. The autopsy showed marked oedema of the brain and small haemorrhages along the vessels in the motor areas of the cortex.

Reflexes. The knee-jerks and abdominal reflexes were notably sluggish in some of the sicker patients. The abdominal reflex was not always obtained. The knee-jerks were present except in Series No. 93, in which the right knee-jerk was sluggish and the left was not obtained, in Autopsy No. 23, in which case there had been pronounced meningeal symptoms, and in two cases in which other signs justified the diagnosis of tabes.

Neuritis was not diagnosed in any case although it may have been the cause of the pain in the shoulder of Series No. 93 or of the weakness of the hands in Series No. 9.

There were no "tender toes." Special efforts were made to avoid pressure of the bedclothes on the toes because this, probably, is the cause of "tender toes" in typhoid.

Hyperaesthesia. One very sick patient was so extremely sensitive that he apparently suffered great pain when touched anywhere. Several other patients at the height of the disease showed a similar hypersensitiveness but of lesser degree. I do not remember having seen this condition so strikingly exemplified in any other disease, although it occurs sometimes in cases of prolonged sepsis and especially after the free use of morphine. According to Gerhard[1] and other writers hypersensitiveness is common in severe cases of typhus.

This symptom was present in slight degree in a fatal case of pneumonia seen recently.

XI. *Pathology of the Nervous System*

Marked cerebral oedema was found in two cases, the only ones in which the brain was examined (*vide* Autopsy Nos. 12 and 23). Both cases have already been mentioned. The first patient had slight renal changes and died in deep coma. The second had tonic spasms of the arms, and, in addition to the

[1] Gerhard: loc. cit.

excess of fluid in the meninges, there were whitish streaks and minute haemorrhages along the vessels in the motor area.

Excess of fluid and more or less oedema of the brain have been observed often not only in typhus but also in other infectious diseases, but no definite relation between oedema and cerebral symptoms has been proven. It is said by older writers to be as common in cases without pronounced cerebral symptoms as in those that have them. The presence of the fluid is sometimes accounted for by the assumption that it replaces atrophy. Until very recently the fluid has not been observed to be under tension. Daniclopolu [1] presents interesting observations on these points.

Cortical haemorrhages, also, have been found in cases that had convulsions but there is doubt whether they were the cause or the result of the convulsions.

Convulsions in typhus may be attributed to cerebral congestion, to haemorrhage or to uraemia (e. g., Autopsy No. 16); but Murchison [2] says that they can sometimes be ended by catheterizing an overdistended bladder.

Inflammatory foci were found in the brain by Prowazek.[3]

Embolism, doubtless, produces hemiplegia in some cases, and thrombus formation in the left side of the heart might account for it.

Among our autopsy cases four at least were comatose for hours or days before death, suggesting cerebral lesions or toxaemia as the primary cause of death. In some cases the coma developed gradually and was not complete until a few hours before death. In other cases it lasted for days. This was so in the cases of Autopsy Nos. 12 and 21. The immediate or secondary cause of death in these two cases seems not to have been the same. The former had a weak and irregular pulse and has already been mentioned in the discussion of the pathology of the circulatory system as a case of cardiac dilatation. The latter showed nothing abnormal about the heart except some fibrous thickening of the mitral valve and there was no pul-

[1] Danielopolu: Le Typhus exanthématique, Bucarest, 1919.
[2] Murchison: loc. cit.
[3] Prowazek: loc. cit.

monary oedema and little, if any, evidence of passive congestion in the viscera. Moreover, the pulse was good until shortly before death. Lesions of the circulatory system and marked derangement of the circulation, therefore, can be excluded as the primary cause of death in this case. Pulmonary lesions can similarly be excluded. Apparently the patient died from cerebral causes with terminal circulatory disturbances.

In two other cases there was marked and increasing pulmonary congestion for several days, probably due to a combination of bronchitis and oedema. Coma developed toward the end. These patients probably died of asphyxia as did the case of Series No. 21 (see "Pathology of Respiratory System"). The pulse in these cases remained good until shortly before death, but the lungs of both showed extensive lesions.

Jurgens[1] attributes death in defervescence or in the afebrile period of typhus to cerebral poisoning rather than to primary cardiac weakness. The writer recognizes that cerebral symptoms may persist in these late stages, but thinks exhaustion more often important as a cause of death at this period (see "Pathology of the Circulatory System").

Gastou[2] says that the epidemic in Serbia was characterized by the frequency and severity of derangement of the nervous system. He found excess of fluid, sometimes clear, sometimes cloudy in the meninges and ventricles; thickening of the arachnoid, cortical ecchymoses, enlargement of the spinal ganglia, and softening of the cord.

The number of our patients having stiffness of the neck and Kernig's sign, or both, is striking. None of the authors quoted mention these signs as being common in typhus. Certainly, however, they are much less frequent in typhoid fever than they were among our typhus patients.

Derangement of the nervous system with coma seemed sometimes to be the primary cause of death, but more often severe general toxaemia with marked secondary circulatory disturbances and extensive pulmonary lesions was followed by coma or deep stupor as its terminal phase.

[1] Jurgens: loc. cit.

[2] Gastou: loc. cit.

XII. *Genito-Urinary System*

Bladder. The sicker patients were always incontinent for a few days before the beginning of defervescence or earlier. As a rule, the bladder emptied itself satisfactorily, but one of my patients required the catheter twice, and another had to be catheterized regularly for several days (Series No. 9 and case of Autopsy No. 24). A third patient, in Dr. Smith's wards, had retention for several days. This patient and the preceding one died.

Murchison [1] says that retention of urine may cause convulsions and that catheterization may stop them.

Urine. Albumen was often found in small quantity, and there were usually a few casts. Tests for acetone and diacetic acid were made in a few cases. They were negative. Acetone bodies, however, have been found occasionally in the urine from cases of typhus. (Curschmann.[2])

An enormously heavy whitish precipitate was noted in the urine which had been standing in a few cases during convalescence. This precipitate was believed to be composed of urates (Series No. 1). Various authors mention this as a feature of convalescence.

The diazo-reaction was performed in a considerable number of cases. It was nearly always positive until the beginning of defervescence when it became atypical or negative.

Haemoglobinuria was suspected in several cases owing to the smoky color of the urine and the absence of blood in the sediment. I have failed to find any author who clearly states that it occurs in typhus. Moore [3] speaks of "a dark color in the urine caused by typhus dissolution of the blood," and Aschoff [4] says that "haemoglobin secretion was found in the kidneys, with haemosiderin pigmentation."

Urobilinuria was found by Michaud [5] in twenty-one out of fifty-eight cases of typhus. I have seen no other mention of it.

Cases of nephritis are described below under "Complications and Sequelae."

[1] Cited by Gastou: loc. cit.
[2] Curschmann: loc. cit.
[3] Moore: loc. cit.
[4] Aschoff: loc. cit.
[5] Michaud: loc. cit.

XIII. *Bones and Muscles*

Pain in the muscles, in the bones or in the joints occurs at various stages of typhus. With the onset of fever, pain in the back and limbs is common, and is said to be nearly as severe as in smallpox. Many of my patients in the early stages of the eruption complained of pain in the legs. It was often associated with sensitiveness of the muscles of the calf, and sometimes of the hamstrings as well.

During convalescence, again, nearly all patients complained of pain in the legs and feet. No objective cause for it was found.

Muscular twitching and spasm has been discussed under the head of the nervous system.

Atrophy of *individual* muscles, most often affecting the deltoid, has been frequently recorded but was not observed by the writer.

In the case of Series No. 9 there was atrophy of the small muscles of the hands.

XIV. *Organs of Special Sense*

Eyes. More or less injection of the conjunctivae was found in practically every case. It seemed to correspond to the flushing of the face and, probably, it often appeared before the eruption. It persisted until the end of the fever, but was most marked at first. Sometimes it covered the conjunctiva, but in other cases it was limited to the part exposed between the lids or to one side of the conjunctiva. Occasionally it was present in only one eye.

Photophobia, if it existed, was slight.

Many authors speak of the "ferret eyes" of typhus, and it is assumed that the comparison has reference to color rather than to any peculiarity of expression, although watchfulness is mentioned by several writers and one of them says that contraction of the pupils is the characteristic of "ferret eyes."

The pupils, as a rule, were not remarkable, but in some cases in the stage of nervous excitement slight contraction was ob-

served, and in a number of patients whose condition was critical pupillary contraction was moderate or even extreme.

Wide dilatation of the pupil followed a few days later but contraction was seen in the case of Autopsy No. 17. Dilatation has been observed as a precursor of death by others, but the writer has no note of its occurrence under these circumstances in typhus.

Pupillary contraction seems to be a rough index of toxaemia.

Corneal ulceration developed in a few cases in spite of care, and all of the patients in whom it appeared eventually died (Autopsy No. 25).

Ears. Bilateral deafness without purulent otitis media is so common in typhoid that it was a surprise to the writer not to find it so in typhus. When deafness was observed it was generally unilateral, and nearly always followed by a purulent discharge from the affected ear. In a few cases there was pain for a few days but no discharge. Deafness is stated by several authors to be very common in typhus.

Herpes on the ears was mentioned above under the head of "Skin."

XV. *Complications and Sequelae*

Urticaria was seen in five or six cases during the febrile period, and was probably caused by unsuitable diet. The food available was far from ideal for febrile patients, and could be supplemented only in part from the special stores of the Lady Paget Hospital.

Erysipelas, starting near the nostril or from a discharging ear, was observed in several cases. In the cases that I saw it was accompanied by little constitutional disturbance and soon cleared up.

Suppurative Lesions. During the convalescent stage abscesses were not uncommon and sometimes they were large. One patient had empyema of the knee-joint, followed by an abscess near the thyroid gland. Perinephritic abscess was a late sequel in one case.

Small boils were common. They sometimes appeared successively, but never in crops.

No case of ulceration in the throat or of noma was encountered among our patients, although Dr. R. P. Strong informed me that at Monastir he had seen cases of this sort.

There were very few bedsores which is remarkable considering the number of patients who were incontinent for longer or shorter periods. Much credit is due the nurses for this.

Parotitis was a frequent complication of the periods of defervescence and convalescence. I saw many cases in other wards but had few in my own. In one of these cases (Series No. 60) unilateral parotitis appeared when the rash was still visible on the body. It developed gradually. The swelling was very hard and but slightly sensitive, improved under poulticing, flared up several times as if about to suppurate, and finally began slowly to disappear. Some swelling still remained when the patient was discharged from the hospital. No incision was required in this case.

In a second case, when the temperature was dropping rapidly toward normal, parotitis first appeared on the right, and on the following day on the left. (Plate XXVI, Figure 1.) Incision on both sides and under the chin was of no avail. The tissues were oedematous and little pus was encountered. The swelling increased rapidly, extended to the glands under the jaw and met underneath the chin. Pain was great, the patient was scarcely able even to swallow liquids. On the sixth day, starting from 100°, the temperature rose steadily to 106.5° on the following afternoon. The patient then died. (Autopsy No. 19.)

All the cases that I saw were characterized by hardness of the swelling and by extreme slowness of recovery. Incision was resorted to in most instances but the amount of pus evacuated was always small.

Suppurative Otitis Media and *Mastoiditis* were observed not infrequently. One patient in the hospital on my arrival had otitis media and signs of meningitis. He died a few days later. Lumbar puncture showed an opalescent fluid with white flocculi in it. The diplococcus of cerebrospinal meningitis was looked for but not found, neither were any other bacteria seen. The case had been diagnosed as typhus, and probably correctly,

although proof of it is lacking. Meningitis is said to be a rare sequel of typhus. Danielopolu's[1] observations on the cerebrospinal fluid are of special interest.

Another patient had otitis and pain in the region of the mastoid followed by purulent discharge from the ear. The other ear subsequently became painful but did not discharge. A third patient had pain and mastoid tenderness of the same character which cleared up without discharge from the ear, and a fourth had a marked secondary rise of temperature associated with pain on attempting to swallow. No abnormality could be seen in the throat, but, after a profuse yellowish discharge had been expelled from the mouth, the patient recovered. A fifth case of typhus, transferred to me in convalescence, had an abscess in the neck originating in the mastoid.

Paresis of the Hands was observed in the case of Series No. 9 during convalescence. Very little motion of the fingers was possible, the grasp became very weak, but improvement was rapid, and when discharged after a protracted convalescence, the patient could use his hands fairly well. The nature of the condition is uncertain.

Cardiac Complications, apparently, were not numerous although a weak and rapid pulse often heralded the approach of death several days in advance. The rate and character of the pulse, the variations in blood-pressure and the pathology have already been described.

Acute endocarditis is regarded as one of the very rare complications of typhus. We had two cases of endocarditis but owing to the lack of data regarding the early part of the illness when a typical typhus rash may have been present, the diagnosis of typhus remains in doubt.

Autopsy No. 2 showed many large, recent vegetations on the valves. In the case of Autopsy No. 26 the lesions were of the small verrucous type and there were few of them.

Thrombus formation in the auricles is generally regarded as not uncommon in typhus so that pulmonary infarction or hemiplegia might result. In two of the cases autopsied by Dr.

[1] Danielopolu: loc. cit.

FIG. 2. THREE CASES OF SLIGHT GANGRENE FOLLOWING TYPHUS FEVER

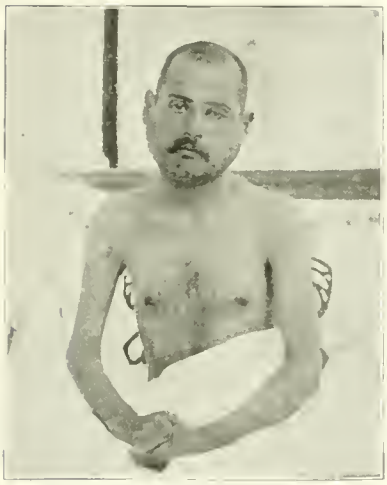

FIG. 1. DOUBLE PAROTITIS
Case of Autopsy Number 19

FIG. 3. GANGRENE AFTER TYPHUS
This case is the one shown on the right in Fig. 2

PHOTOGRAPHIC ILLUSTRATIONS OF CASES AT LADY PAGET HOSPITAL
(From photographs presented by Dr. Sellards)

PLATE XXVI

Zinsser mural thrombi were found in the apex of the left ventricle. These thrombi were believed to have originated before death, but of this Dr. Zinsser was not quite certain. (Autopsy No. 4.)

Phlebitis of a mild type is believed to have existed in the case of Series No. 47. In the case of Autopsy No. 8 a typical pulmonary infarct was found.

Vascular Complications. *Gangrene* of the feet seems to have been very common during the cold months in the early part of the epidemic. Dr. Strong said that he saw many cases of gangrene in some of the hospitals and that in some cases the nose or ears were affected.

Maitland [1] made some interesting observations on it. He noted that before gangrene appeared the feet and hands became blue and cold and the pulse "thready," i. e., small and weak, that red patches of hyperaemia then appeared on the feet, and that gangrene developed in the areas which had become thus congested. Reasoning from the fact that a part once frostbitten remains for some time afterwards sensitive to exposure he inferred that frostbite or exposure incidental to warfare may have played a predisposing part by injuring the vessels.

That this form of gangrene is not embolic is evidenced by its frequent symmetry. Moore [2] believed that gangrene results from arterial thrombosis, but it seems probable that Maitland is right in supposing that exposure may be a factor in its production. Another factor which was probably operative during the early months and particularly in some localities is lack of nursing. The feet of the patients may have been allowed to remain cold for long periods during the illness when the circulation was sluggish, or the circulation may have been handicapped by leaving the boots on. In the presence of some of these predisposing factors local infection may have aided in the formation of a thrombus, or its development may, perhaps, have been determined by changes in the walls of smaller arteries such as Prowazek [3] found in those of the skin.

[1] Maitland: loc. cit. [2] Moore: loc. cit. [3] Prowazek: loc. cit.

Gangrene heals very slowly. It seems to develop most often in the later stages of typhus or during convalescence. Consequently there were many old cases of it in the wards when we began work. Others were brought in after the rash had disappeared. Typical instances, slight in degree, are shown in Plate XXVI, Figures 2 and 3.

Whether or not all the cases of gangrene which we saw were in reality due to typhus it is impossible to say with certainty. During the summer, few cases of gangrene developed in the hospital and none in my wards. The comparative scarcity of gangrene at this period was due apparently to two causes: firstly, warm weather; and secondly, good nursing.

Series No. 33a was brought in with severe gangrene, and several other patients admitted at the same time had cold, discolored feet which looked as if about to become gangrenous, but the circulation was restored by the application of heat locally. Special care was taken with all typhus patients to keep the feet warm and to avoid pressure upon them even by the blankets.

Pulmonary Complications. Bronchitis and passive congestion were so common as to be considered features of ordinary typhus rather than complications. Both were found in most of the cases that came to autopsy.

Pneumonia. The dyspnoea during life often suggested pneumonia, and in cases of this sort faint bronchial breathing could sometimes be found in the back, but at autopsy definite consolidation was seldom discovered.

There was extensive lobar consolidation in only one instance (Autopsy No. 7).

In Autopsy No. 25 bronchopneumonia was caused by inhalation of food.

Two probable cases of bronchopneumonia with recovery were mentioned above under the head of "Sputum." (Series No. 93.)

Capricious localization of intense haemorrhagic oedema in several cases suggested the possibility that pneumonia was developing. The condition in question was found in the case of

Autopsy No. 18. It was localized at the *top* of the right lower lobe. In this case the ordinary signs of passive congestion were absent. In Autopsy No. 9 a similar condition existed at the base of the left lung, and in Autopsy No. 20 it was combined with passive congestion of the ordinary type.

Pleuritis. Extensive pleuritic adhesions, some old, some more recent, and others obviously fresh were found in many cases. No typical friction rub was heard, but pleuritis probably accounted for some of the pain in the chest which was complained of not infrequently.

A fresh haemorrhage was found on the pleural surface of the lung at the right apex in the case of Autopsy No. 4, and in that of Autopsy No. 8 there was a recent infarct.

Pulmonary gangrene. Typical pulmonary gangrene developed during convalescence in the case of Series No. 59 mentioned above under "Respiratory Signs and Symptoms."

Pulmonary gangrene may be caused by embolism from septic areas (Murchison [1]) or by inhalation of septic material from perichondritis of the larnyx (Curschmann [2]).

Renal Complications. The urinary sediment during the febrile period, in the case of Series No. 1, indicated nephritis by the presence of many hyaline, granular, and fatty casts and compound granule cells. There was little albumen, however, and the condition of the urine improved rapidly during convalescence. A renal irritation of less degree, which scarcely requires to be classified as a nephritis, was found in another case. The urine showed in this case a specific gravity of 1024, a trace of albumen, many granular casts, and a few red blood-cells.

In the case of Series No. 9 the urine was like that in Series No. 1, but the patient subsequently developed oedema of the face and legs, and the nephritis seemed to be passing into a chronic form when the patient was discharged.

In the case of Autopsy No. 16 there was a chronic nephritis which undoubtedly antedated the typhus, and there were also acute kidney changes attributable to the typhus. This patient died in a convulsion, probably of uraemic origin.

[1] Murchison: loc. cit. [2] Curschmann: loc. cit.

In a number of other cases slight fatty degeneration of the kidney was found at autopsy. Curschmann [1] says that most authors regard acute nephritis as a comparatively frequent complication of typhus. Among our cases well marked evidence of nephritis was rare, but signs of more or less renal irritation, such as is common in severe febrile diseases, were frequently present.

XVI. *Convalescence*

Even after the most severe symptoms, convalescence was rapid considering the emaciation and weakness of the patients. The gain of strength from day to day, the improvement in appearance, the increased ability to assimilate food, and the increase of mental activity was rapid as compared with typhoid.

Frequently patients whose temperatures had not yet reached normal would sit up in bed and ask either for solid food, or to be sent home on furlough. Some patients were fit for discharge after a week of normal temperature. Those who had been very ill were kept longer in the hospital because discharge often meant walking to their homes which were, perhaps, many miles away.

Pain, more or less severe, in the legs and feet was a very common symptom of convalescence.

Slight recurrences of temperature often terminated promptly after a cathartic had been taken.

In a few cases rapidity or irregularity of the pulse persisted for a considerable time.

XVII. *Diagnosis*

The differential diagnosis of typhus may be discussed by taking up the various stages of the disease separately.

Stage of Invasion. Before the appearance of the eruption influenza may easily be mistaken for typhus or *vice versa* on account of the conjunctival injection, the redness of the pharyngeal mucous membrane and of the tonsils, and the slight signs of coryza associated with symptoms of general infection.

[1] Curschmann: loc. cit.

Siebert,[1] who studied typhus recently in a camp of Russian prisoners, says that there were at first mild illnesses like influenza, which were followed later by cases of undoubted typhus with more severe symptoms. He had the impression that among the early influenza-like cases there were some cases of abortive typhus. Similar cases of mild typhus were observed toward the end of the typhus epidemic.

The experience of Jurgens[2] among Russian prisoners was like that of Siebert.[1] He says that just before the typhus epidemic they had influenza to deal with, but that when the typhus appeared there was no more influenza.

During the same epidemic in Hungary, Wiener[3] observed mild cases of typhus like those described by Siebert.[1] He says that the febrile period may last from three to six days and that the disease is like influenza except that often there are chills at the beginning or during the course of the fever. In other cases he observed headache, malaise, nasal catarrh and cough, and sometimes angina from ten to fourteen days before the outbreak of "the real disease."

Apparently, influenza may prepare the way for typhus or may go with it in the same epidemic as relapsing fever so often does.

These observations are of special interest to the writer because at the end of the epidemic in Serbia we saw many cases of transient fever which were thought at first to be influenza, but later, the question of pappataci or "three-day fever" was raised. Dr. Castellani, who was familiar with this disease, said there were many cases of pappataci fever in the town close by at that time.

The cases in question at the Lady Paget Hospital showed injection of the conjunctivae, flushing of the face, and catarrh of the respiratory passages. Some of them also had transient eruptions. When first seen the patients said they had been ill two days. They complained of malaise, headache, and pain in the back and limbs. On the third day, as a rule, the temperature fell abruptly to normal.

[1] Siebert: loc. cit. [2] Jurgens: loc. cit. [3] Weiner: loc. cit.

It would seem that to distinguish between abortive cases of typhus, pappataci fever, and influenza may be extremely difficult because there is no doubt that typhus infection may appear in a very mild form, and that such cases are likely to appear at the beginning or end of an epidemic. It is possible, therefore, that some of our patients with supposed pappataci fever may really have had abortive typhus. The appearance of a rash in several of these cases strengthens that hypothesis.

The fact that "influenza-like" bacilli were found in the sputum of two cases of undoubted typhus, and that in one of these cases they were very numerous (see "Respiratory Signs and Symptoms," above), points to the probable coexistence of influenza infection among our patients at the time when the doubtful cases were developing.

The bacilli in question were described as "influenza-like," not because they differed from the bacillus of influenza in size, shape, or staining reaction, but because their identity was not confirmed by cultivation. The observations of Wiener,[1] Siebert,[2] and Jurgens,[3] made during the same epidemic of typhus in another locality, increase the probability that influenza and not pappataci fever may have been the real cause of some of the mild cases in question. If so, mild typhus, influenza, and pappataci fever apparently prevailed at the same time. Series Nos. 88 and 100 are included to illustrate difficulties of diagnosis.

Inasmuch as some epidemics of "influenza or grippe" have proven to be really due to pneumococcus bronchitis still another possible source of error in diagnosis suggests itself. Series No. 100, just mentioned, was a case of pneumococcus bronchitis.

Another important fact is that influenza cannot be entirely excluded because of the presence of an eruption. Not many years ago in Paris an extensive epidemic prevailed which was finally diagnosed as influenza although many of the patients had an eruption which resembled that of typhus (Wagener[4]).

[1] Weiner: loc. cit.
[2] Siebert: loc. cit.
[3] Jurgens: loc. cit.
[4] Wagener: Med. Klin., xv, No. 25.

Relapsing fever may be confused, in the beginning, with the stage of invasion of typhus. In typical cases, the onset of relapsing fever is more abrupt than in typhus, the temperature rises much more rapidly, goes higher, and the constitutional symptoms are slight in comparison with the fever. Conjunctival injection, if present, is slight, but the face may be flushed and its appearance may be strikingly like that of typhus. Enlargement of the spleen is easily demonstrable in relapsing fever.

Relapsing fever, in a number of cases, developed during convalescence from typhus. It may have preceded it in others.

Tertian malaria and aestivo-autumnal malaria caused no great difficulty in differential diagnosis. These cases became numerous as the summer advanced.

The onset of smallpox is said to resemble that of typhus.

Stages of Nervous Excitement and of Nervous Depression. The presence of a well-marked eruption having the usual distribution and character of typhus was considered sufficient for a positive diagnosis, but when atypical rashes were seen, as in Series Nos. 88 and 100, it was believed that a diagnosis of typhus could not be made with anything like certainty. When, also, the subsequent course of the disease was atypical the diagnosis remained in doubt. Criteria based on the degree of severity of symptoms or on the course of the fever can have little value for recognition or exclusion of abortive typhus. No sign or symptom of typhus was nearly so characteristic as the eruption. When the eruption was well developed the disease ran a course which varied little.

If there are cases of typhus in which no rash is present at any time, it would seem extremely difficult to diagnose such cases with certainty, even during an epidemic of typhus, because of the various other diseases that may be prevalent at the same time.

Murchison [1] says that if there are cases of typhus without even a transient eruption they must be very rare.

The diagnosis of "typhus without eruption" has been made not infrequently by some persons on the ground that the prog-

[1] Murchison: loc. cit.

ress of the cases resembled typhus in other respects and that the patients were known to have been exposed to this infection. Having seen no such case I am skeptical of the diagnosis of "typhus without eruption."

If there were cases of typhoid among my patients I failed to recognize them although this disease was always borne in mind. There should be no difficulty in distinguishing typhoid from typhus when the eruption is well marked and typical, but, after a transient or scanty eruption has disappeared, doubt may arise.

Typhus with eruption on the face, as in the case seen by Dr. Sellards, might bring measles into question. The subsequent course of the fever and the characteristic changes in the rash, however, would soon settle the diagnosis.

The Widal reaction has lost much of its value for diagnosis since antityphoid inoculation has become such a common practice. Moreover, McClure [1] says that a positive Widal reaction in low dilutions is common in typhus. Clumping occurred in a few of our typhus cases at a dilution of 1 in 25. Agglutination tests for paratyphoid A and B were always performed with the Widal test. They were uniformly negative.

The bites of fleas and of other vermin, when numerous, may resemble an eruption, or may confuse the picture when an eruption also exists. Similarly, scabies may mask a rash or even lead to an erroneous diagnosis of typhus fever. (Series No. 33.)

The case of Series No. 88 presents a particularly complex combination of skin lesions. Drug eruptions, a profuse crop of rose spots in typhoid, haemorrhagic eruptions in the acute exanthemata and skin lesions in secondary syphilis, plague or influenza may require to be differentiated from typhus. The spots of purpura, cerebrospinal meningitis or acute endocarditis are not likely to cause difficulty.

The association of scurvy with typhus, which has been observed in some epidemics, and the possibility of combined infection of typhus with typhoid, dysentery, diphtheria, relapsing fever, or the exanthemata should be borne in mind.

[1] McClure: Handbook of Fevers, N. Y., 1914, p. 321.

Stage of Defervescence. Diagnosis at this stage depends on the exclusion of typhoid fever, relapsing fever, tuberculosis, malaria, and Malta fever, of which we had two probable cases, and on the presence of reasonably characteristic remains of the eruption. The recognition of this was discussed in the section on "Skin."

At this stage, also, acute endocarditis may come into question because heart murmurs are generally present in the later stages of typhus. The cases of Autopsy Nos. 2, 11, and 26 illustrate the difficulties of late diagnosis.

When, during a typhus epidemic, a patient is brought in with gangrene of the leg (Series No. 33a), or with parotitis following a fever of many days duration, it is probable that the lesions are sequelae of typhus; but, whereas they develop sometimes also in other infectious diseases a diagnosis can scarcely be made with certainty in cases of this sort after the rash has disappeared.

XVIII. *Treatment in General*

As a basis for rational treatment the causes of morbidity and of mortality require to be understood.

It is certain that filth, famine, overcrowding, and lack of ventilation favor the spread of typhus. They favor it not only by increasing opportunity for transmission of infection but also by weakening in advance the resistance of the person infected. Notwithstanding some apparently contradictory evidence, it seems certain that bad conditions of living tend to lower the resistance of the individual and to increase morbidity as well as mortality in an epidemic of typhus.

The first fundamental principle of treatment rests on these facts. It demands *maintenance of the patient's remaining strength by every possible means* (1) by removal from unsanitary surroundings (2) by good nursing, and (3) by a well-regulated diet. These points are elaborated below.

Fresh air and cleanliness are certainly beneficial. It is probable, therefore, that suitable tents would make better wards than ill-ventilated rooms. Maxwell [1] says that the Italians in

[1] Maxwell: Brit. Med. Jour., 1915, No. 1, p. 528.

Tripoli preferred to use tents or huts for the sake of ventilation and ease of destroying vermin.

Good nursing saves the patient needless suffering, and helps very much to maintain strength.

It is probable that parotitis, ulcerative lesions of the mouth and throat, otitis media, and external infectious processes including bedsores can be prevented in most cases by a skillful nurse if she has sufficient time to do her work thoroughly; and that hypostatic congestion, pulmonary complications, and gangrene of the extremities will be far less common among her patients than among those lacking such care.

The kind and quantity of nourishment should be suited to the *digestive capacity of the individual* and must vary with the stage of the illness and the nature of the symptoms. The effort should always be made to administer the greatest quantity of nourishment that the patient can digest. Liquid nourishment only can be taken by the sicker patients, but when soft solids can be taken they should be administered. Good judgment is needed to get the best results. Therefore the physician should personally supervise the dietary.

The methods advocated above are important not only to combat pre-existing weakness in cases admitted late in the disease, but also to counterbalance the exhaustion and loss of flesh incidental to typhus in its severer forms. Prostration is more often extreme in typhus than in any other similar disease. A most striking fact is the occurrence of many deaths *after the period of defervescence* even when severe complications have not developed. It is probable that extreme exhaustion, with attendant depression of vital functions and consequent inability to recuperate, is the essential factor in the fatal result in most of these cases (Autopsy Nos. 13 and 14). That exhaustion is also an important factor in many deaths which occur *during defervescence*, and in some that occur still earlier, seems extremely probable (Autopsy Nos. 9 and 24).

Maintenance of strength, therefore, seems to be important at all stages of typhus as a means of saving life. That this principle is of special importance for the treatment of middle-aged

or elderly patients is suggested by statistics of mortality. It is known that, after the period of childhood, percentage mortality increases steadily with advance in years, and that it becomes extremely high in elderly persons. Murchison's [1] Diagram II based on more than 18,000 cases demonstrates the truth of this statement.

It is not possible to determine the stage of the disease at which death occurred in all of our cases which were autopsied but more than a third of the fatalities (seven at least) occurred after defervescence from the primary fever. In at least five of these cases the dominant factor seemed to be exhaustion. Death in the sixth case was from parotitis and sepsis, and in the seventh case from exhaustion and pneumonia. In three of the earlier deaths exhaustion seemed to play an important part (Autopsy Nos. 6, 9, and 24).

Inasmuch as a large proportion of patients die after having passed the acute period of typhus it is clear that efforts to conserve strength should not be relaxed until after the patient has made decided improvement.

Nasal feeding was used in several patients who were unable or unwilling to swallow enough food. It served well in several cases that might not have recovered otherwise. Unfortunately, one delirious patient, who struggled against the feedings and in whose case they were tried as a last resort, developed inhalation pneumonia.

The place of alcohol in the treatment of typhus is an important question.

When a patient is rapidly losing strength because he cannot assimilate food, I believe that alcohol should be administered, not in small doses, but freely. Alcohol has been abused in the past, and many now deny that it has any value, but they are probably mistaken.

In suitable cases alcohol acts apparently as a food which is readily absorbed, and capable to a considerable degree of replacing other nourishment. If this is true, it is important that the indications for administering alcohol should be clearly understood.

[1] Murchison: loc. cit.

Gerhard [1] on the subject of typhus says: — "In the later stages of fever, wine, porter, and in a few cases even brandy were given with much benefit. It is difficult to conceive the extreme prostration in which our patients were left after a severe attack of fever. The skin is usually cool and the pulse weak and fluttering, but there is still muttering delirium and great feebleness. Under these circumstances, wine, combined with quinine, and a nutritious diet produced an effect which was almost magical." "The amount of wine given in twenty-four hours varied from 4 to 16 ounces. It was generally from 6 to 8 ounces. Practitioners have remarked that a moderate dose of wine is capable of producing all the good effects which can result from it. In our observations a similar result was obtained, and we rarely exceeded eight ounces daily except as a temporary prescription to *obviate extreme prostration. The quantity given with that object was not limited but was increased until the strength of the patient improved.*" "Where the fever was higher and the prostration less, wine became less useful. *We therefore restricted its employment to the periods of prostration, when it was indispensably necessary.*" (The italics are mine.)

Stokes [2] taught that where there was faintness of the heart sounds at the apex and weakening of the cardiac impulse with a pulse which was rapid and of poor quality, alcohol was required; but he took into consideration also the state of nutrition of the patient. Two cases, described by him in Chapter XXVIII of his book, show that he used alcohol very freely in the presence of extreme prostration and emaciation. He advises against its free use when there is "active irritation of the brain," but says that alcohol may be tried even then if circumstances demand.

Murchison [3] complained of the indiscriminate use of alcohol common in his day and doubted the wisdom of administering more than twelve ounces of brandy in twenty-four hours under any circumstances, but he valued alcohol too. He says that most patients over forty are benefited by alcohol from the commencement of the second week or earlier, that persons of in-

[1] Gerhard: loc. cit. [2] Stokes: loc. cit. [3] Murchison: loc. cit.

temperate habits require alcohol earlier and in greater quantity than others, that the *chief indication for the use of alcohol is derived from observation of the pulse and heart as stated by Stokes, and that the more the typhoid state is developed the more will alcohol be needed.* Slowing of the pulse under alcohol and diminution of delirium were regarded as evidence of beneficial effect and *vice versa.* Other indications for alcohol were coldness of extremities and a dry, brown tongue. Profuse perspiration without contemporaneous improvement indicated a need for more alcohol, and a hot, dry skin or scantiness of the urine were considered as contra-indications for alcohol.

The question of whether alcohol was a food or a stimulant troubled Murchison [1] and he concluded to call it a stimulant.

Indications for the use of alcohol in *typhoid fever* were given by F. C. Shattuck [2] as follows: — "If the heart shows distinct signs of undue weakness, if hypostasis is threatened or marked, if the power to take, retain, or appropriate nourishment is unduly lowered, I believe it to be a grave error in judgment to withhold alcohol." If alcohol is useful in typhoid it is needed more often for the same indications in severe typhus.

Dr. F. C. Shattuck has taught that "*in acute infections, especially toward their later stages, the toleration of alcohol may be greatly increased over that of health, and that it may then render inestimable service, notably when the power of taking or assimilating food is greatly impaired.* No measured limit can be set down for its use. No more should be given than is burnt up, combustion being determined by the presence or absence of the smell of alcohol on the breath, in combination with the symptoms of the patient, and the influence upon the latter apparently exerted by the alcohol."

To discuss experimental evidence as to the effect of alcohol on nutrition, circulation, respiration, etc., would be out of place in this paper but a few facts may be stated. It is well known that a certain quantity of alcohol is quickly absorbed, and readily oxidized in *the healthy body*, that it can supply some of

[1] Murchison: loc. cit.

[2] Shattuck, F. C.: Therapeusis of Internal Diseases, Forchheimer, N. Y., 1913, ii

the energy ordinarily derived from carbohydrate or fat, and that, in so doing, it prevents the destruction of body tissue which ensues when the quantity of fat or carbohydrate ingested is insufficient for requirements. Less is known of its action in disease of various kinds.

It is reasonable to suppose, however, that the beneficial effects of alcohol in ill-nourished patients are due in large measure to energy supplied by the alcohol, and that, when the patient is exhausted and emaciated, alcohol by acting as a food may increase vital energy and thus indirectly improve circulation and respiration. It is the experience of Dr. F. C. Shattuck, as stated above, that conditions may occur in disease which greatly increase the power to assimilate alcohol.

Patients under my care received alcohol in considerable quantities and apparently with benefit. It may, at least, be said that no typhus patient died in my wards after the period of high fever except from severe complications.

The earlier the stage of typhus, the less prominent seems to be exhaustion as a cause of death. It may, however, be an important factor in exceptional cases as it seems to have been in the case of Autopsy No. 9.

The principal cause of early death when it occurs in typhus is toxaemia. There may be lesions in the heart and other organs, but severe functional disturbances without corresponding known lesions seem to be the direct result of toxins circulating in the blood. Some of the older writers have denied that cerebral congestion and oedema are the cause of cerebral symptoms, claiming that these occur to the same degree in cases in which cerebral symptoms were not marked, and that the excess of fluid merely replaces atrophy of brain tissue. Quite different views have been expressed by Danielopolu [1] in his recent book on typhus. More light is needed on this question.

The second fundamental principle in the treatment of typhus is based on the belief that toxaemia is an important cause of death and that, therefore, it should be combated in every possible way.

[1] Danielopolu: loc. cit.

Toxaemia in typhus can be attacked by attempting to dilute the toxin in circulation, by promoting its elimination, or, according to Danielopolu,[1] by neutralizing or destroying the toxin in the blood by means of intravenous injections of chlorinated salt solution. This last method was unknown when this paper was originally written.

Circulating toxin can be diluted by the administration of abundant water by mouth. When sufficient water cannot be ingested it can be given in the form of enemata, or as salt solution by hypodermatoclysis or intravenously. These methods were used freely.

They caused marked increase in the excretory activity of the kidneys and seemed also to improve the circulation. Thus, they may have benefited the patient by diluting toxin and by favoring its elimination through the kidneys both directly and indirectly.

The question of how much liquid should be ingested by the patient daily in acute fevers has not been settled. McCrae[2] advocates three liters per diem as a minimum in typhoid, prefers five or six liters, and has administered much larger quantities. It may be asked whether this internal hydrotherapy, when carried to extremes, may not cause disturbances which more than counterbalance its benefits. For example, may it interfere with digestion? May it put undue strain on the heart in cases in which the heart is weak? May it, in typhoid, increase the frequency or severity of intestinal haemorrhage?

In typhus the possible danger of overtaxing the heart by rapidly administering very large quantities of fluid should be borne in mind because the heart muscle seems more often to be weak in typhus than in typhoid fever. On the other hand, damage to the heart and blood-vessels might be minimized by ingestion of large amounts of liquid if begun early in the disease.

The bowels should receive special attention in typhus, a disease in which constipation is the rule, in order to prevent absorption of toxins from them. Slight recurrences of fever in convalescence frequently yield promptly to free catharsis.

[1] Danielopolu: loc. cit. [2] McCrae: Modern Medicine, ed. by Osler, Phil., 1907.

When, in typhus, the face becomes cyanotic, the breathing rapid, and signs of general toxaemia are well marked it seems probable that moderate purgation with a saline cathartic, such as magnesium sulphate, may have a beneficial effect. There is a striking resemblance between some of these cases and certain instances of influenza with bronchopneumonia which were treated in France in the autumn of 1918. Purgation seemed in these cases of bronchopneumonia to be definitely beneficial. Whether the improvement resulted from elimination of toxic material or otherwise is uncertain. It may have benefited the heart by reducing the volume of the circulating fluid.

XIX. *Symptomatic Treatment*

Among symptoms of a serious nature in our cases of typhus were those of circulatory insufficiency. This condition seemed to be the contributing cause of death in most of the fatal cases. Less often it was regarded as the principal cause of death.

Digitalis was administered in all cases in which the pulse became weak and irregular or the pulse rate rose above 120 per minute. The dose by mouth varied from 0.2 to 0.4 gram daily. In several instances bradycardia was thought to have been caused by the digitalis (Series No. 83). It seems impossible to tell whether or not the patients would have done as well without the digitalis.

A number of patients had occasional sudden attacks of circulatory weakness from which they rallied promptly after administration of whisky by mouth, a drink of hot tea or soup, or a subcutaneous injection of strychnin, camphor in oil, or ether. During these attacks the patients seemed to be in an alarming state of collapse. The pulse was extremely weak or even imperceptible. The recovery was prompt and striking. One patient recovered, however, before anything had been administered, so that doubt is cast on the value of the treatment used for the others. The patient referred to in Autopsy No. 24 had many such collapses before he died.

I am not prepared either to attach much value to these methods of cardiac stimulation or to deny them all value, but

incline to the belief that they may, in some cases, produce transient reflex rise of blood-pressure which may have a temporary beneficial effect. For example, we know that pain causes a temporary rise of blood-pressure. A subcutaneous injection, therefore, may act through pain even if the substance injected is medicinally inert. Locally irritating substances like camphor or ether probably act mainly in this way.

As a heart stimulant strychnin has no demonstrated value. It was not used by me for this purpose. The work of Richard C. Cabot and the more recent studies of Newburgh [1] throw light on this subject.

When a patient had had one attack of circulatory collapse it was found that another might be expected to follow. The nature of circulatory insufficiency in typhus has already been discussed under "Pathology of the Circulatory System" where reasons were given for believing that the disturbance originated sometimes in the vascular system and sometimes in the heart. More often, apparently, the two kinds of disorder were combined.

Salt solution was administered intravenously in a number of cases of different types. In the cases in which the circulatory disturbance seemed to be mainly due to vascular relaxation the response was gratifying.

In the case of Series No. 9 the circulation improved repeatedly after the infusions, and life seems to have been prolonged by them for several days until a favorable turn of the illness was followed by recovery.

Salt solution by intravenous infusion was used also in the cases of Series Nos. 10, 59, and 93, and in the cases described under Autopsy Nos. 24 and 25. In the case of Series No. 10 the infusion gave little benefit. During the second injection temporary improvement of the pulse was followed by signs of heart weakness which made it necessary to stop the procedure. A slight rigor followed soon after the injection. Infusions were used in the case of Series No. 59, not to improve the pulse, which was fairly good, but to replace fluid lost by diarrhoea

[1] Newburgh: Am. Jour. Med. Sc., 1915, xlix, 696; Arch. Int. Med., 1915, xv, 458.

and to prevent expected circulatory collapse. The first injection did good. The second was soon followed by transient weakness and irregularity of the pulse. This time the solution may have done more harm than good. In the case of Series No. 93 two infusions were given. Both were followed by rigors. Nevertheless, even in this case, the effect on the whole may have been beneficial. After the rigors were over the patient's condition was more satisfactory than it had been before the infusion was administered.

In the case of Autopsy No. 24 the first infusion caused a marked temporary improvement in the circulation but transient violent delirium followed, and, later, another circulatory collapse occurred. A second infusion given several hours afterwards called forth little circulatory response. This case seemed to be one of the sort which is hopeless from the beginning.

Autopsy No. 25 is a somewhat similar case. Salt solution improved the pulse in this case but delirium increased and a rigor took place. After the second infusion, morphine was injected, no rigor occurred, and the pulse remained satisfactory for twenty-four hours after administration of the salt solution.

The cause of the rigors which so often followed infusions of salt solution in my cases is not clear. Apparently, they were not due to errors of technique because they were not prevented by the most careful preparation of the solution, by using freshly distilled water, or by carefully maintaining a warm temperature of the solution while it was being administrated.

It is of special interest that Castelloi (quoted by Doty [1]) administered normal salt solution several times daily in the dose of 250 to 300 c.c. totalling from 600 to 1800 c.c. per day in 136 cases; and that he had only 9 deaths under this regime as against 13 deaths in 113 patients under "purely symptomatic treatment."

Sponge baths served to reduce temperature, but no very certain benefit resulted.

When there was marked pulmonary congestion and bronchitis no form of treatment seemed to relieve the patient. It is

[1] Doty: loc. cit.

difficult to see what, beyond general measures, can be done for such cases. The frequently existing acute inflammation of the bronchial mucosa would seem to contra-indicate the use of "stimulating" expectorants. Atropine might be expected to make the condition worse by increasing the viscidity of the secretion and thus preventing its expulsion. The associated bronchitis, when severe, contra-indicates morphine because it prevents expectoration.

The urine should be watched for signs of nephritis and appropriate modifications of diet should be instituted when there is evidence of nephritis.

The stools should be inspected, especially when there is diarrhoea, to see if the food is being well digested. Curds of undigested milk are a frequent cause of diarrhoea in typhoid fever.

The prevention of complications was spoken of above under "Treatment in General" and nursing. Special attention should be paid to the mouth and throat. The legs and feet should be kept warm, and pressure on the feet, even from the bedclothes, should be avoided lest it contribute to the production of gangrene.

At first sight the treatment for gangrene of the toes might seem to be amputation, but Dr. Smith informed me that, even when amputation was performed rather high, the gangrene sometimes recurred. When the gangrene was not extensive he preferred to keep his patients in bed and to wait for recovery by spontaneous separation of the dead tissue. The process was slow but loss of substance was surprisingly small and the results were excellent. When pieces of bone had been exposed they sloughed off and the skin grew over the stumps.

It seems possible that pituitrin might be useful in cases of circulatory collapse in typhus. Having none it was not tried.

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Series Number 1. *Diagnosis:* Typhus fever, moderately severe; with mild acute nephritis.

Clinical Notes

Austrian prisoner, age 30, working as a mason, admitted to the hospital on April 23.

April 24. Present Illness: For three days fever, constipation, and loss of appetite. No vomiting. Pain in the eyes began early and persists. Deafness in the right ear began yesterday. There is no coryza or sore throat. Bowels moved four times last night after calomel. There is pain in the left knee and calf, but none in the back.

Physical Examination: The patient is well developed and nourished. There is a bright flush over the malar region and a slight suffusion of the eyes. The tongue is moist and shows a moderately heavy white coat. The throat is negative. There is no glandular enlargement.

Heart: Dulness not increased, action rapid, rate 92. The pulmonic second-sound is louder than the aortic second-sound. The first-sound at the apex is indistinct. A soft systolic murmur is heard in the pulmonic area. The pulse is large and bounding, the vessel walls soft, and the blood-pressure, 115 S.–50 D.

Lungs: Negative.

Abdomen: Full and soft, not sensitive to pressure.

Liver and *Spleen:* Not palpable, but the splenic dulness is increased.

Reflexes: The right abdominal is present, but that on the left is indefinite. The knee-jerks are present.

Calf Muscles are sensitive to pressure.

The Eruption consists of pink macules varying in size, irregular in shape, disappearing on pressure, profusely and uniformly distributed over the trunk, legs, and arms. A few are seen on the backs and soles of the feet. The hands and the face are free from spots. There are some bright pink spots on the scalp.

April 25. The eruption seems more profuse on the body and some spots no longer disappear on pressure. The general color of the rash is purplish. Spots have appeared on the backs of the hands.

The mind is clear, and the expression phlegmatic. In the afternoon the patient vomited some greenish fluid and had pain in the abdomen. The bowels moved three times today. The coat on the tongue has become yellowish. There is no cough. The abdomen is soft and not sensitive. Haemoglobin (Tallquist), 95 per cent. White count, 24,000. Urine: normal in color, acid, sp. gr. 1016, albumen a trace, no sugar, diazo-reaction present. Sediment: coarse granular casts.

April 26. The eruption is clearly visible on the palms of hands. Many spots on the body are still pink and disappear on pressure. A few others have begun to turn brown. The mind is clear and the expression brighter.

April 27. Mentally duller today: complains of weakness, heaviness in the head and pain over the eyes. Slight Kernig's sign present. Attempt to flex neck does not cause pain but the neck is slightly stiff. The pupils are of normal size.

The Calf Muscles are slightly sensitive to firm pressure.

The Sputum is viscid and frothy with yellowish streaks.

Urine: A 24-hour mixed specimen is light, but slightly smoky in color, acid, sp. gr. 1015, albumen a slight trace, no sugar, diazo-reaction positive. Tests for acetone or diacetic acid were negative. The sediment shows many granular casts. The quantity of urine has increased.

April 28. Blood: White count, 12,000; haemoglobin (Sahli), 120 per cent, (Tallquist), 100 per cent; red count, 4,000,000; color index, 1.75; differential count:—polymorphonuclears, 92 per cent, large mononuclears, 4 per cent, other types, 4 per cent. The red cells appear normal. The platelets are scarce.

Heart: The sounds are rather feeble. The first-sound is short. The blood-pressure is 65/S.–50/D.

The tongue is dry, and the face bronzed and dusky. There is moderate loss of flesh. The eruption is purple and brown. The patient is drowsy but his mind is clear.

Urine: Normal in color, acid, sp. gr. 1010, albumen a slight trace. The diazo-reaction is positive. The sediment shows many hyaline, granular, and fatty casts, and compound-granule and other cells.

May 2. There has been a gradual fall in pulse rate and temperature for the past four days with slow improvement in the general condition of the patient.

Heart: The sounds are of good quality, the pulse rather small and soft, the rate 95. The nails and lips are slightly cyanotic, and the face and ears are dusky in color. Blood-pressure, 80/S.–60/D.

The patient complains only of frontal headache. He looks comfortable and placid as always. The color of the face is distinctly darker than at the time of admission. It seems to be more pigmented. White count, 16,000.

May 3. The diazo-reaction is negative.

May 4. Heart: The first-sound is blurred and faint, and the second-sounds are of good quality. Blood-pressure, 90/S.–50/D.

The injection of the conjunctivae is practically gone.

May 6. Haemoglobin (Tallquist), 85–90 per cent. Blood-pressure, 100/S.–60/D.

The eruption is fading but brown mottling remains distinctly visible.

Urine: Normal in color, sp. gr. 1018, no albumen, the diazo-reaction is negative. The sediment shows a very large quantity of amorphous material which is readily dissolved either by heat or by acid. This sediment was believed to be composed of urates.

White count, 10,700.

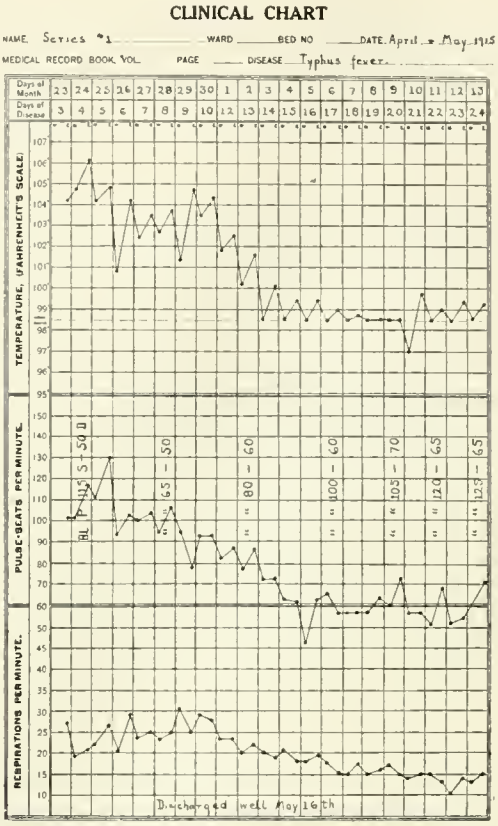
May 8. Digitalis was ordered after the patient had been in the ward a few days. It was omitted today because the pulse rate fell to 48.

Urine: Normal in color, sp. gr. 1019, no albumen, many hyaline casts.

May 9. Heart action regular and slow. The pulmonic second-sound is accentuated and louder than the aortic second-sound. The second-sound at the apex is accentuated. The first-sound is almost replaced by a soft systolic murmur which is heard also in the pulmonic area but is not transmitted to the axilla. Blood-pressure, 105/S.–70/D. Haemoglobin (Tallquist), 85 per cent. White count, 7200.

May 11. The eruption is brownish, with a faint purplish tinge. It is still clearly visible on the body and arms.

Heart: The pulmonic second-sound is accentuated, and louder than the aortic second-sound. The second-sound at the apex is accentuated. The



Series Number 1. Typhus fever moderately severe; with mild, acute nephritis. Admitted to hospital April 23, 1915. Haemoglobin estimations, red counts, white counts, and blood-pressure are recorded on the chart

first-sound is obscured by a systolic murmur which is not transmitted to the axilla. Blood-pressure, 120/S.–65/D.

Urine: Normal in color, neutral, sp. gr. 1012, no albumen, rare hyaline casts.

May 13. The first-sound is still blurred. Blood-pressure, 125/S.–65/D. Haemoglobin (Tallquist), 65 per cent. The eruption is pale pinkish brown in color.

May 16. The Widal test and agglutination tests for paratyphoid A and B were negative in dilutions of 1 to 25 and 1 to 50.

The patient was discharged from the hospital in excellent condition.

SERIES NUMBER 9. *Diagnosis:* Typhus fever, severe, with nephritis apparently becoming chronic.

Clinical Notes

Serbian, age 30, admitted to hospital on April 26.

April 27. Present Illness: The patient says that he has been ill for three days. The color of the rash suggests that he has been ill at least a week but he may have worked until three days ago.

Physical Examination: The patient is moderately emaciated, the face browned by the sun, the malar region flushed, the eyes hollow, the nose sharp and the facies typical of typhus. The skin is dry, and the conjunctivae are moderately injected. The tongue has a slight brown coat. The nostrils move with respiration and the breathing is rapid and rather deep. Muscular twitching of the hands is frequent.

The eruption is scanty on trunk and legs and more marked on the arms and hips. It is macular and punctiform in character and purple in color. The face, the backs of the hands and those of the feet show no spots.

April 28. Heart: The action is rapid and regular. All heart sounds are accentuated. No murmurs are heard. The pulse is small and weak.

Lungs: Many fine râles are heard in the back, especially at the bases. There is no dulness and the breath sounds are normal.

The abdomen is concave and soft.

The abdominal reflexes are lively and the knee-jerks are very sluggish. The neck is moderately stiff and Kernig's sign is present to a slight degree. The muscles of the left calf are sensitive to pressure.

There is muttering delirium at times and the patient is not fully conscious. The facial expression is that of pain. Gestures indicate pain in the forehead and in the legs. The breathing is very rapid.

The Urine is of normal color, acid, sp. gr. 1015, and shows a trace of albumen. The test for sugar is negative. The sediment shows many granular and fatty casts.

April 29. The body is emaciated and the skin is dry.

Heart: The sounds this morning are of poor quality, and the pulse is very weak. The systolic blood-pressure is 70 mm.

The patient is conscious but mentality clouded and his movements are tremulous. He has a frequent, dry cough.

This morning about 720 c.c. of salt solution were given intravenously. The pulse rate dropped from 140 to 120 while the first 500 c.c. were going in and the pulse improved much in quality at the same time. The injection

was terminated later because the pulse rate rose again to 130, and its quality deteriorated. The heart sounds, however, remained excellent. At 5 P.M. the heart sounds were clear, the action regular, and the rate 134. The blood-pressure was 75/S.–60/D., and the pulse small and weak. At 6 P.M. salt solution was again administered. The pulse improved much at first during the injection, but after about 480 c.c. had been given the patient coughed repeatedly, the heart sounds which had been abnormally loud became less so, and the pulse deteriorated again. The patient did not look quite so well and seemed rather prostrated. Therefore the injection was discontinued.

The blood examination made one hour after the first infusion of salt solution showed a haemoglobin (Sahli) of 125 per cent, a red count of 5,500,000, a white count of 4000, and a color index of 1.13.

April 30. This morning the patient is weaker and semicomatose. He slept better, however.

The pulse is of very poor quality but the heart sounds are fairly good. In the afternoon the pulse was much stronger for a time, but weakened again later. Salt solution was administered at 6 P.M. and again at midnight in small amounts with good effect.

May 1. The pulse is of fair quality this morning and the heart sounds are good.

The temperature has dropped abruptly to normal and the pulse rate has fallen to 92. Muscular twitching persists.

May 3. This morning the patient is semicomatose and can only be roused with difficulty. The pulse is very weak and irregular in force. After about 720 c.c. of salt solution had been given intravenously at 11 A.M. the heart sounds became loud. The blood-pressure was then 95/S.–70/D.

May 4. The patient looks rather dried up this morning, but feels well enough to smile.

The heart sounds are loud and the pulse is of fair quality, the rate being 70.

The temperature has remained normal for 24 hours. The respiration rate has varied from 20 to 24 during the past three days.

May 5. Patient passed only about 15 c.c. of urine today. The bowels moved once today and three times freely yesterday. The abdomen is markedly distended and is tympanitic. It shows slight general tenderness. There is no dulness in the region of the bladder.

The nurse says that the patient frequently takes from 240 to 300 c.c. of liquid at a time. She reports also that at times the pulse is slow and of poor quality. Since the administration of a little brandy one hour ago it has been excellent. The heart sounds are now of good quality and the rate moderate. Digitalis was then prescribed.

The patient seems mentally dull and physically weak.

Shortly after the time mentioned in the last note an enema was given with little effect on the bowels but soon the patient voided about 720 c.c. of urine and the abdominal distention nearly disappeared.

May 6. The patient is better this morning. For the past three days he has been asking for bread.

The pulse is of good quality and the blood-pressure is 90/S.–60/D.

There is no distention. Patient is taking 240 c.c. of water every two hours and eating well. His face is less emaciated. Haemoglobin (Tallquist), 90 per cent.

The urine is acid, the sp. gr. 1025, and the diazo-reaction is negative. The sediment shows many hyaline and granular casts, some of them with fat and cells adherent.

In the afternoon the left side of the face on which the patient had been lying was distinctly oedematous.

May 7. The face and eyelids are slightly swollen and there is slight oedema of left leg. The patient is very drowsy. Muscular twitching and cough have stopped. Limitation of the ingestion of liquid was prescribed.

Digitalis was discontinued on account of bradycardia.

May 9. The right side of the face is still slightly swollen. The patient is weak and drowsy. The bladder is distended nearly to the umbilicus. The patient was, therefore, catheterized. Haemoglobin (Tallquist), 90 per cent. Blood-pressure, 100/S.–80/D.

May 11. The patient now urinates normally. He is gaining strength. There is no oedema. The ingestion of liquids has been limited to 1000 c.c. in 24 hours.

The aortic second-sound is accentuated, and is louder than the pulmonic second-sound. The first-sound is faint and blurred. Blood-pressure, 105/S.–65/D.

May 14. The patient is passing more urine and his condition is improving steadily.

The heart action is slow and regular, the pulmonic second-sound is accentuated and louder than the aortic second-sound. The second-sound at the apex is accentuated, and the first-sound is nearly replaced by a systolic murmur which is heard equally well in the pulmonic and mitral areas, and is not transmitted to the axilla. Blood-pressure, 105/S.–70/D. Haemoglobin (Tallquist), 75 per cent.

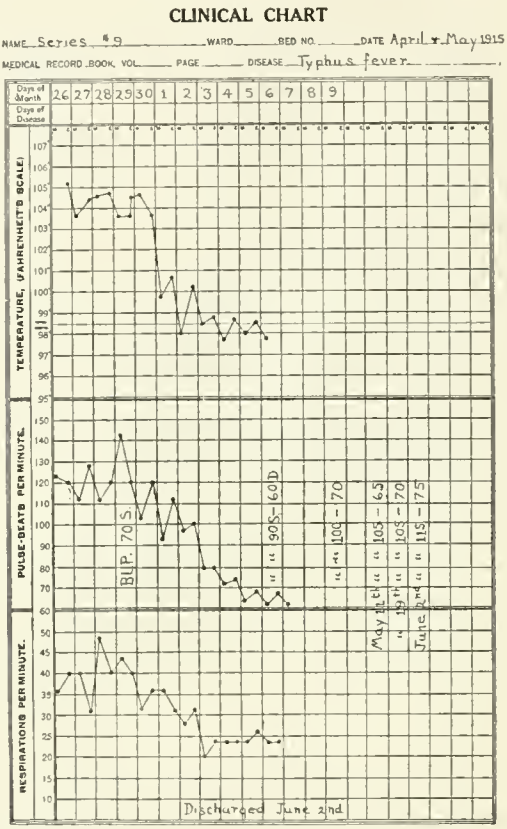
May 26. The Widal test and the paratyphoid A and B agglutination tests are negative in dilutions of 1–25 and 1–50.

May 30. The urine is normal in color, the sp. gr. 1008, and there is no albumen.

The general condition of the patient is good.

The fingers were almost completely paralyzed for a time but their strength is returning.

June 2. The second-sounds of the heart are now of good quality. The pulmonic second-sound is louder than the aortic second-sound. The first-sound is blurred by a systolic murmur which is heard all over the precordia. It is loudest in the mitral area and is not transmitted to the axilla. It disappears when the patient sits up. The cardiac dulness is slightly increased



SERIES NUMBER 9. Typhus fevere severe. Nephritis apparently becoming chronic. Admitted to hospital April 26. Haemoglobin estimations, red counts, white counts, and blood-pressure are recorded on the chart

to the left and the apex impulse, when the patient lies on the left side, is felt in the mid-axillary line. Its force is greater than normal. Blood-pressure, 115/S.–75/D.

The lungs are negative. The skin and mucous membranes are abnormally pale. Haemoglobin (Tallquist), 75 per cent.

The patient is much stronger. He was discharged today, advice having been given about diet with regard to signs of nephritis.

Series Number 10. *Diagnosis:* Typhus fever moderately severe with marked irregularity of the pulse.

Clinical Notes

Serbian, age 37, admitted to hospital on April 26.

April 27. The patient is said to have been sick for three days, but more probably he has been so for a week.

Physical Examination: The patient lies on the side. He is apathetic but mentally clear when aroused. He then becomes nervous and excitable. There is a malar flush, the eyes are sunken, the conjunctivae are injected, there is moderate emaciation, and the skin is dry. The pupils are large, equal, and react to light. The tongue shows a white coat. The throat is red. There is no glandular enlargement.

The eruption consists of scattered pink or purple macules on the chest, abdomen, and back. The face, the arms and the legs show no eruption. The pink spots disappear on pressure, and the purple ones fade, but do not disappear.

Heart: The dulness is normal and the action regular but slightly rapid. The aortic second-sound is muffled and the pulmonic second-sound is faint. The sounds at the apex are of poor quality and the pulse is soft.

The Lungs are negative.

The Abdomen is concave, soft, and not tender. The liver and spleen are not palpable.

Reflexes: The abdominal reflexes are absent, but the knee-jerks are present. The neck is moderately stiff and there is a slight Kernig's sign.

The calf muscles are not sensitive to pressure. On the left hip is a purple spot about 6 cm. in diameter, due probably to pressure.

Treatment: Ordinary care and cathartics were prescribed.

April 28. The face which is much browned by the sun has a tinge of cyanosis. The patient is fully conscious but drowsy.

The palms of the hands are bright yellow in color and the soles of the feet are slightly yellow.

The systolic blood-pressure is 80 by palpation. By auscultation it varied from 90 to 70 but there were heart beats which gave no sound in the artery which shows a marked irregularity of force. The haemoglobin (Tallquist) was considerably above 100 per cent.

Urine: Color high, acid, sp. gr. 1016, albumen a very slight trace, diazo-reaction strongly positive.

April 29. Temperature falling. General condition about the same, pulse weak.

Haemoglobin (Sahli), 130 per cent, red count, 5,900,000, color index, 1.10, white count, 16,600, platelets scarce; differential count: polymor-

phonuclears, 72 per cent, lymphocytes, 8 per cent, large mononuclears, 17 per cent, transitional cells, 2 per cent, unclassified, 1 per cent.

April 30. Lungs clear. Sputum frothy, white, very viscid. Pulse of poor quality in the morning, better in the afternoon. Salt solution was administered by rectum.

May 1. The heart sounds are of poor quality. The aortic second-sound is very indistinct but the second-sound at the apex is fairly loud.

May 2. The patient is better this morning.

The pulse has been irregular in force and rhythm ever since admission and the heart sounds have been of poor quality most of the time. This evening at 6 P.M. the pulse rate at the wrist had risen from 110 to 120. The heart rate at the same time was 132. The face was markedly flushed and there was slight cyanosis of ears, face, and finger nails.

Heart dulness to the right was slightly increased.

The patient has been getting salt solution by rectum every six hours and had 720 c.c. yesterday afternoon intravenously. It was administered because the skin was very dry and the body emaciated as if in need of liquid. Last night 240 c.c. of salt solution were given intravenously, but the infusion was then stopped because the heart sounds had become faint, and because the pulse rate had not diminished. The pulse had improved, however, in quality. Shortly after the infusion the patient had a slight rigor. Nothing of this sort followed the first infusion.

Blood: White count, 14,200, haemoglobin (Sahli), 100 per cent, red count, 5,900,000.

May 3. This morning the patient is decidedly better.

The aortic second-sound is faint, but the pulmonic second-sound is good. The first and second-sounds at the apex are excellent. Blood-pressure, 85/S.–55/D.

May 4. The patient is much brighter.

The heart sounds are of good quality. Blood-pressure, 90/S.–60/D.

There is considerable cough with scanty, viscid expectoration. The conjunctivae are still injected. The tongue is clean. White count, 9700.

May 5. Urine: Color normal, sp. gr. 1017, albumen a very slight trace.

May 6. A few days ago the patient complained of pain in the tip of the right middle finger. A small, red, purpuric spot was seen under the skin. Following this there was swelling of the finger tip. Yesterday a little pus was evacuated by incision.

The general condition of the patient is improving steadily. The entire face and ears have been flushed and are so still. The conjunctivae are no longer injected.

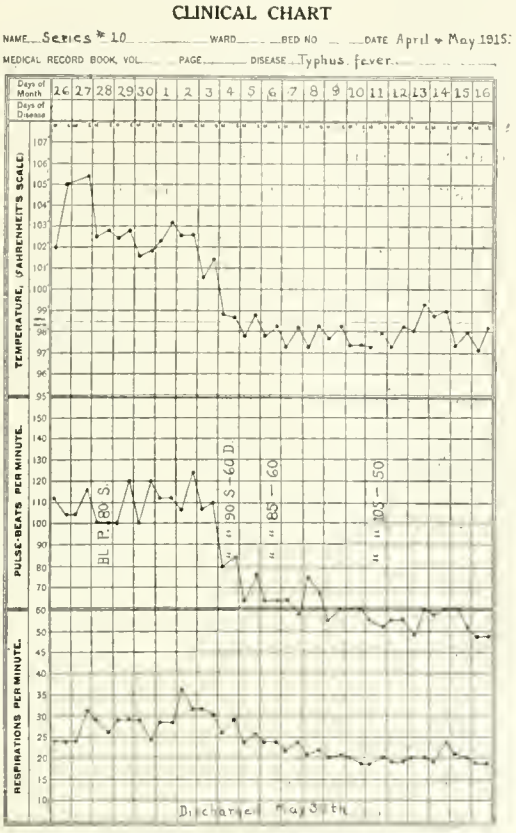
Herpes appeared on the ear several days ago.

Blood-pressure, 85/S.–60/D. Haemoglobin (Tallquist), 80 per cent. White count, 6300.

May 7. Haemoglobin (Sahli), 100 per cent. Red count, 4,700,000.

May 8. Urine: Color high, acid, sp. gr. 1023, albumen a slight trace.

May 9. The heart action is regular, and slow. The aortic second-sound is louder than the pulmonic second-sound. The first-sound is blurred by a faint systolic murmur. Blood-pressure, 95/S.–60/D. White count, 5700.



Series Number 10. Typhus fever, moderately severe with marked irregularity of the pulse. Admitted to hospital April 26. Haemoglobin, red counts, white counts, and blood-pressure are recorded on the chart

Digitalis was omitted yesterday morning, and the brandy which the patient had been having for several days was omitted a few days earlier.

May 11. Haemoglobin (Tallquist), 100 per cent.

The heart sounds are of good quality. The pulmonic second-sound is louder than the aortic second-sound. A systolic murmur is heard over the precordia, loudest in the mitral area, and not transmitted to the axilla. Blood-pressure, 105/S.–50 D.

May 13. The face is desquamating.

The pulse is of good volume and tension. The pulmonic second-sound is louder than the aortic second-sound and both are accentuated. The first-sound is blurred by a systolic murmur. The second-sound at the apex is accentuated. Blood-pressure, 100/S.–55/D.

Today the patient was out of bed for the first time.

May 19. The patient's condition is improving rapidly.

The heart action is slow and the sounds are of good quality except the first-sound which is faint. The pulse is small. Blood-pressure, 100/S.–60/D. Haemoglobin (Tallquist), 80 per cent.

May 30. The urine is normal in color, sp. gr. 1018, no albumen. The patient was discharged today in excellent condition.

SERIES NUMBER 36. *Diagnosis:* Mild typhus. Bradycardia, no drugs used.

Clinical Notes

Serbian, age 26, admitted on April 26.

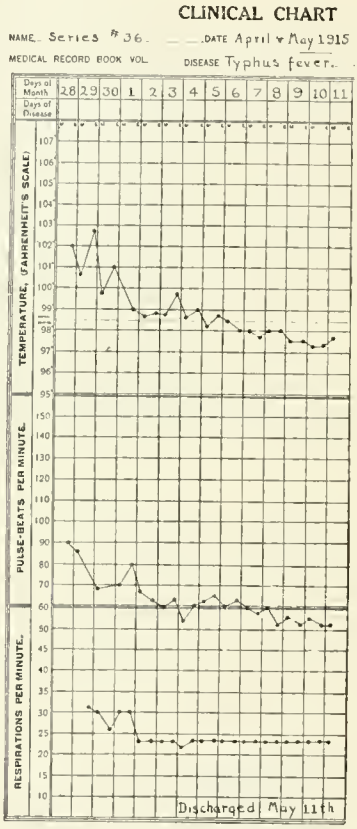
April 26. Said to have been ill ten days.

April 28. Urine: Normal in color, acid, sp. gr. 1017, no sugar, albumen a slight trace. The sediment shows a rare hyaline cast.

Eruption Present: A complete examination was not made because the condition of the patient was satisfactory and other work pressing.

May 8. The tongue is clean. The conjunctivae are injected on the right side of each eye but not on the left side. The skin shows a few spots of doubtful nature. The patient is gaining rapidly in strength and his state of nutrition is good but he looks anaemic. Haemoglobin (Tallquist), 80 per cent. Blood-pressure, 120/S.–55/D.

May 11. The patient was discharged as cured.



SERIES NUMBER 36. Typhus fever, mild. Admitted to hospital April 26. Bradycardia. No drugs were prescribed

SERIES NUMBER 48. *Diagnosis:* Typhus fever; with chronic cervical adenitis and hysteria during convalescence.

Clinical Notes

Serbian, age 30, admitted May 12, by transfer from the Fourth Hospital to which he went for cervical adenitis eighteen days ago.

May 12. Physical Examination: On the right side of the neck is a considerable swelling due to enlarged glands embedded in swollen, indurated tissue. In this region there is a discharging sinus which is not draining freely. There is an enlarged gland beneath the jaw. This swelling is moderately sensitive.

The tongue shows a white coat, the teeth are good, and the pillars of the fauces and the soft palate are slightly red. There is a single dark red papule on the inside of the right cheek. The patient is tremulous and breathes rapidly. There is an occasional hard cough. The sputum is scanty and consists of frothy, viscid, blood-streaked mucus. The entire face and ears are hyperaemic, the malar region not more so than the rest.

The eruption is rose-red in color and chiefly macular in character. There are a few papules. They are not petechial. The spots are numerous on the chest, abdomen, and back; fewer on the arms, legs, and feet; and absent on the hands and face.

The heart action is regular. The pulmonic second-sound is slightly accentuated and louder than the aortic second-sound. The first-sound is of good quality. The pulse is of good volume and fairly good tension. The systolic blood-pressure is about 100. Pressure from the inflated cuff of the instrument caused the arm to twitch so that an accurate reading was impossible.

The lungs show a few scattered, fine and coarse, moist râles.

The abdomen shows no tenderness or reflex spasm but there is voluntary rigidity. The spleen is not palpable but splenic dulness is slightly increased.

The knee-jerks are present. The calf muscles are slightly sensitive to pressure. Kernig's test shows slight spasm of leg muscles and causes pain. The neck is stiff and there is pain when passive flexion is attempted. Haemoglobin (Tallquist), 90 per cent.

May 13. The heart sounds are of good quality and the pulmonic second-sound is louder than the aortic second-sound. The blood-pressure is 95/S.–80/D.

May 15. The heart sounds are all loud, but are obscured by coarse râles. Blood-pressure, 115/S.–60/D. There is considerable cough but the secretion is less viscid. The temperature, pulse, and respiration are falling and the patient looks better. Haemoglobin (Tallquist), 70 per cent.

May 16. White count, 16,000.

May 19. The temperature was normal last night. The swelling on the neck and the local tenderness have diminished much under poulticing.

The heart sounds are loud and of good quality. A faint, systolic murmur is heard in the mitral and pulmonic areas. Blood-pressure, 105/S.–65/D. Haemoglobin (Tallquist), 90 per cent.

May 21. White count, 3000.

June 2. The patient's condition has improved rapidly since the temperature touched normal. The nutrition has been well maintained.

Yesterday the patient walked outdoors and fell down but sustained no apparent injury. Today his happy smile is gone and he shakes all over when approached. The knee-jerks are much exaggerated. He walks with a limp, but can walk without it. The patient had a similar nervous disturbance a week ago following an operation done in the ward on a man with parotitis. The disturbance is clearly hysterical. When eating his meals the patient appears perfectly well. After reassurance and sitting outside on the steps for a little while, he regained his normal condition.

The glands in the neck remain hard, but there is much less swelling, and the sinus is smaller. There is no discharge now.

Blood-pressure, 115/S.–75/D. Haemoglobin (Tallquist), 90 per cent.

The patient was discharged in good condition early in June.

The adenitis was better but not cured.

Series Number 49. *Diagnosis:* Typhus fever; typical case of moderate severity.

Clinical Notes

May 13. Serbian soldier, admitted to hospital today, says he has been ill in barracks four days and complains of pain in forehead, eyes, and legs.

Physical Examination: Well developed and nourished. The breathing is rapid and accompanied by grunting and movement of the nostrils, but the patient breathes deeply and without effort. There is a hard dry cough. Answers to questions are intelligent and prompt. The pupils are equal and of moderate size, the conjunctivae are deeply injected, and the tongue shows a heavy, white coat. The teeth are good, the pharynx and pillars of the fauces are bright red, and the tonsils are enlarged.

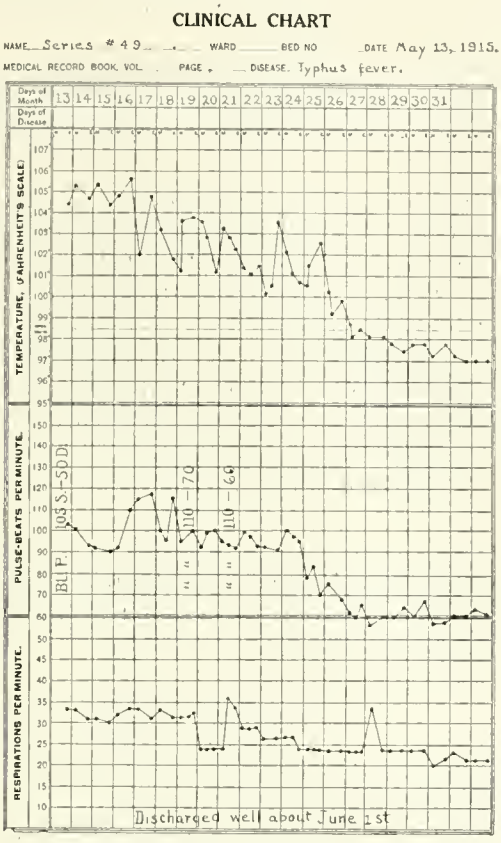
Glands: The epitrochlear glands are barely palpable; those in the axillary and inguinal regions are not enlarged, and the posterior auricular glands are not palpable.

The whole face and the upper part of the neck are flushed. The suffusion is brightest on the ears and in the malar region.

Eruption: There is on the face one papule and several minute purple spots which might be old flea bites. There are many macules on the chest, the back and the arms, and a few on the neck, hands, legs, and upper abdomen, but none on the lower part of the abdomen. The rash consists

chiefly of macules but there are also some papules resembling the rose spots of typhoid, and a few punctate purple spots, undoubtedly flea bites.

Heart: The action is regular and rather rapid, the aortic second-sound is accentuated and louder than the pulmonic second-sound. The



Series Number 49. Typhus fever — a typical case of moderate severity. Haemoglobin, white count, and blood-pressure are recorded on the chart

first-sound is loud but blurred. The second-sound at the apex is accentuated. Cardiac dulness is normal. Blood-pressure, 105/S.–50/D.

Lungs: A few coarse râles are heard.

Abdomen is soft and shows slight, general sensitiveness. The spleen is not palpable but splenic dulness is increased. *The knee-jerks* are present. The calf muscles and hamstring muscles are sensitive to pressure. Kernig's test causes pain. The neck is very slightly stiff. Haemoglobin (Tallquist), 85 per cent.

May 15. The eruption is beginning to turn purple but most of the spots are still pink.

The heart sounds are all of good quality, the aortic second-sound equals the pulmonic second-sound and the pulse is of the bounding type. Blood-pressure, 105/S.–60/D. Haemoglobin (Tallquist), 70 per cent.

May 16. White count, 12,800.

May 19. There has been a rapid fall of temperature associated with steady improvement in the condition of the patient. The nutrition is well maintained. The eruption is turning brown. The leg muscles are no longer sensitive.

The second-sounds are accentuated, especially the pulmonic second-sound. The first-sound is of fair quality, the pulse is full and soft, and the blood-pressure is 110/S.–70/D. Haemoglobin (Tallquist), 95 per cent.

May 21. The patient is doing well. Blood-pressure, 110/S.–70/D. Haemoglobin (Tallquist), 75 per cent.

May 26. The convalescence is rapid. Blood-pressure, 110/S.–60/D. Haemoglobin (Tallquist), 90 per cent. The Widal test in dilution of 1–25 is positive but in that of 1–50 it is negative. Agglutination tests for paratyphoid A and B are negative at 1–25 and 1–50.

The patient was discharged well about June 1.

SERIES NUMBER 57. *Diagnosis:* Typhus fever; persistent vomiting in convalescence, and bradycardia. Four-hourly temperature chart, showing crisis.

Clinical Notes

May 17. A Serbian, age 20, admitted yesterday afternoon; and said to have been sick twelve or thirteen days.

Physical Examination: The patient lies on his side sleeping comfortably. The breathing is rather rapid and deep but the nostrils do not move. When aroused the patient grunts occasionally when breathing.

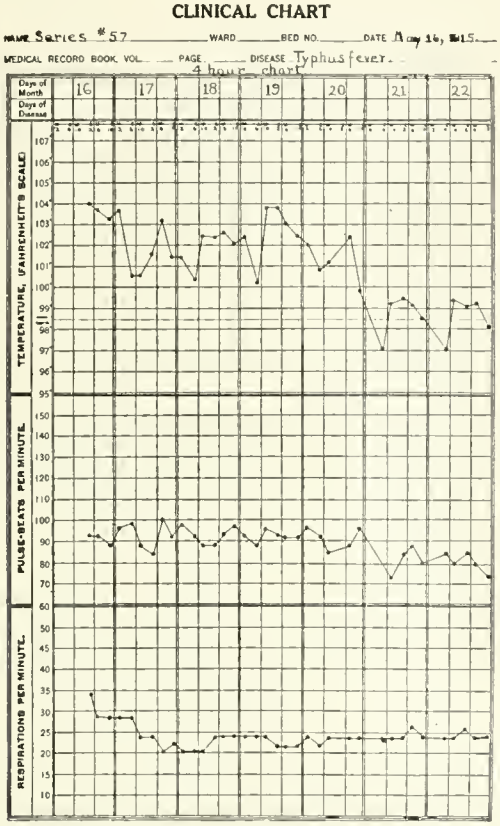
The face is brown and slightly flushed especially in the malar region. The ears are particularly red.

The pupils are equal and of normal size, the conjunctivae moderately injected, the tongue shows a white coat, and the throat is slightly red.

The Eruption is macular. The spots are irregular in shape and of various sizes. Their color is purplish or bluish pink. There are a few spots on the neck, legs, and back, and many on the shoulders, upper chest, flanks, and abdomen. The face, mucous membranes, hands and feet show no spots.

The Heart Action is regular and not rapid. The aortic second-sound is accentuated, and the pulmonic second-sound much accentuated and louder

than the aortic second-sound. The first-sound is blurred by a systolic murmur which is heard also in the pulmonic area but is not transmitted to the axilla. The second-sound at the apex is slightly accentuated. There is a



Series Number 57. Typhus fever; four-hourly chart showing crisis

marked pulsation in the neck. An excessive pulsation is seen in the second and fourth interspaces over the heart.

The heart impulse is increased in force and is best felt in the fourth interspace in the mid-clavicular line. When the patient lies on the left side an excessive impulse is felt in the fourth interspace in the mid-axillary line. No murmurs are heard. Blood-pressure, 110/S.–85/D.

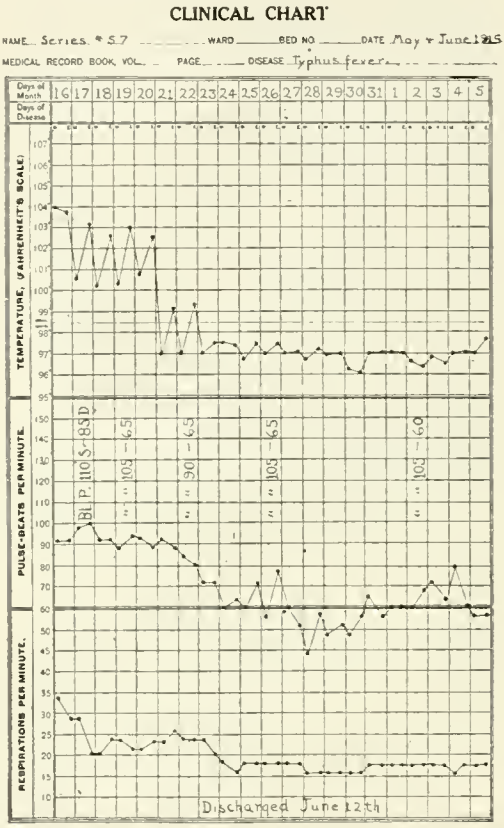
The Lungs are negative.

The Abdomen is flat, soft, and not sensitive. Pressure causes gurgling, especially in the right iliac fossa. The liver and spleen are not palpable and the splenic dulness is not increased.

The neck is slightly stiff and there is a slight Kernig's sign but the test does not cause pain. The leg muscles are not sensitive. The knee-jerks are present.

Haemoglobin (Sahli), 110 per cent, red count, 4,600,000, white count, 7800, color index, approximately 1.30.

Treatment: Routine without drugs.



Series Number 57. Typhus fever; persistent vomiting in convalescence, bradycardia, crisis

May 19. All the second-sounds are accentuated and especially the pulmonic second-sound. The pulse is full, and the blood-pressure, 105/S.–65/D.

The eruption is fading and turning brown. Haemoglobin (Tallquist), 95 per cent.

May 22. The patient is very thin. He has vomited frequently. (No drugs have been used.)

The second-sounds are accentuated, especially the pulmonic second-sound. The first-sound is of fair quality. The second-sound at the apex is accentuated and the pulse is of fair quality. Blood-pressure, 90/S.–65/D. Haemoglobin (Tallquist), 90 per cent.

May 23. The patient still vomits everything. Examination of the abdomen is negative. Calomel was prescribed yesterday in small, repeated doses and feeding was attempted in very small quantities every hour but the patient vomited even water. Nutritive enemata and salt solution by rectum were prescribed.

May 26. The patient has not retained the salt solution well and has continued to vomit until yesterday afternoon when he was able to keep down a little water. This morning he has taken 240 c.c. of liquid nourishment and looks better.

The heart sounds are of good quality, the pulmonic second-sound is accentuated and louder than the aortic second-sound. The second-sound at the apex is accentuated and the first-sound is of good quality. Blood-pressure, 105/S.–65/D.

June 2. Improvement is marked and rapid.

June 11. There is now no stiffness of neck or legs. The patient is very thin, but is fairly strong. Blood-pressure, 120/S.–65/D. He will be discharged tomorrow.

Series Number 59. *Diagnosis:* Typhus fever; diarrhoea, crisis, pulmonary gangrene in convalescence.

Clinical Notes

May 19. Serbian, age 22. He says that his left eye became inflamed about twenty days ago and that he has had fever for seven days. There has been no pain except in the eye.

Physical Examination: The patient is well developed and fairly well nourished. He is fully conscious and mentally clear. The face is brownish, the cheeks moderately flushed, and the forehead slightly so. The ears and nose are red.

The right pupil is very large, but it reacts to light. The left eye is inflamed and sticky. The tongue shows a whitish coat, the throat is red, and the tonsils are slightly enlarged.

The glands in the axillae are enlarged but the posterial auricular glands are not palpable.

Eruption: The face and mucous membranes are free from spots. There are a few spots of doubtful nature on the neck. On the arms, the chest, and the backs of the hands there are a few typical, pink spots which disappear on pressure. On the abdomen there are a few macules and

papules. Macules are seen faintly outlined on the legs and feet. The back shows many reddish papules of doubtful nature.

The Heart Action is regular and rapid. The pulmonic second-sound is accentuated, and louder than the aortic second-sound. The second-sound at the apex is accentuated. The first-sound is blurred by a systolic murmur which is loudest in the pulmonic area and is not transmitted to the axilla. The pulse is of the bounding type. There is excessive pulsation in the neck. The arteries are soft. Blood-pressure, 125/S.–45/D.

The Lungs are negative.

The Abdomen is soft, full, and not sensitive. The spleen is palpable about 4 cm. below the costal margin and the splenic dulness is much increased.

The Neck is decidedly stiff but an attempt at flexion does not cause pain. The neck muscles are not sensitive. There is a definite Kernig's sign without sensitiveness of calf or thigh muscles. The knee-jerks are present. Haemoglobin (Tallquist), 95 per cent.

Routine treatment and brandy in small quantities were prescribed.

May 21. White count, 3900.

May 22. The patient is losing weight rapidly although taking nourishment well. His color is not good, the pulse is of poor quality. Blood-pressure, 105 S.–50/D. Haemoglobin (Tallquist), 75 per cent.

Digitalis and extra diet were prescribed.

May 23. The patient is taking nourishment well but continues to lose weight and strength. His condition is critical. The eruption has become profuse all over the body and limbs, and is turning purple.

Nutrient enema of syrup, 60 c.c. in 480 c.c. of water were administered every six hours.

May 26. Urine: Color high, neutral, sp. gr. 1012, no albumen, diazo-reaction strongly positive.

May 28. The patient began to have diarrhoea yesterday and it became profuse to day. The stools are of the pea soup variety, and not offensive. There is incontinence of the bowels.

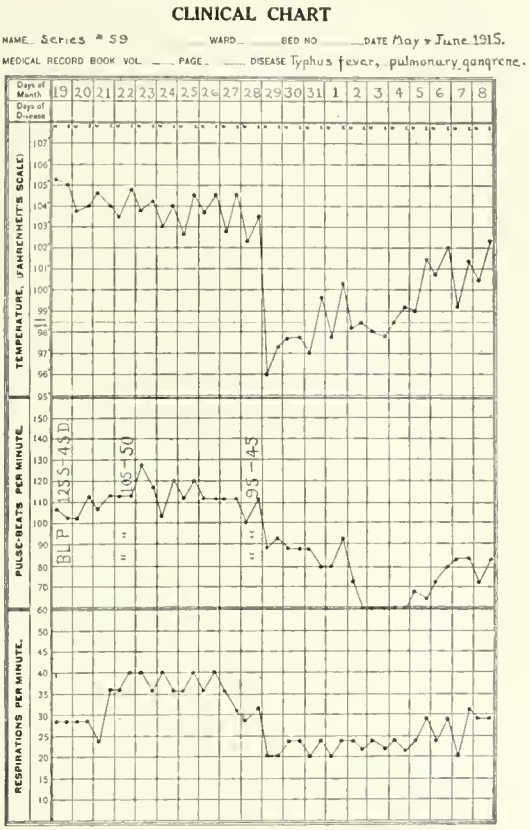
The mouth has been very foul. The nurse says it has required cleaning hourly.

The patient is mildly delirious, picks at the bedclothes, and is extremely weak.

The pulse has remained full and of good quality. Blood-pressure at 6 P.M. 95/S.–45/D. The aortic second-sound is faint and the pulmonic second-sound of fair quality. The first-sound is faint and second-sound at the apex is accentuated.

May 29. The patient's condition was so bad yesterday evening that he was not expected to live through the night. He was extremely weak and seemed too tired to breathe, but the pulse continued pretty good. Salt solution, 480 c.c., was given intravenously in the evening with benefit.

This morning after the crisis, the patient's condition is still bad. Although the pulse was satisfactory, salt solution was given again intravenously to make up for fluid lost by diarrhoea. Fifteen minutes after the infusion the pulse became very weak and irregular, and the patient seemed about to die.



Series Number 59. Typhus fever; severe diarrhoea, crisis, pulmonary gangrene in convalescence

The pulse afterwards improved slowly, and in the evening it was decidedly better.

June 2. Opium was used for a few days to check the diarrhoea, but the stools then became foul. The opium was consequently discontinued, the quantity of food was reduced, and castor oil administered. Today the patient seems out of danger. He has a small black patch over the sacrum which appeared about the time of the crisis but which, probably, will not slough.

June 11. Since June fourth there has been gradually increasing irregular fever with slight constitutional symptoms.

About the time of the crisis and for several days the patient was extremely sensitive all over. Any motion or attempt at motion caused great pain.

Examination today with the patient lying on the left side shows a few râles at the left base behind and slight sensitiveness in the *right flank* without spasm. The patient's appearance suggests tuberculosis. He has been raising much sputum which is frothy and tenacious.

June 12. Urine: High colored, sp. gr. 1013, no albumen or bile.

June 24. The sputum became foul about a week ago and a small area of dulness with a few râles was found at the *right base* in the axilla. The râles at the left base meanwhile disappeared.

Moderate elevation of temperature persists. The sputum continues to be raised in considerable quantity and is foul at times. More often it is frothy and inoffensive. Microscopic examination shows no tubercle bacilli. There are great numbers of Gram-negative influenza-like bacilli, besides bacteria of many kinds, and a few pneumococci and spirochaetae.

The patient remained in the hospital on account of these pulmonary symptoms and had periods of improvement followed by exacerbations. He was last seen about the end of August still in the hospital.

Series Number 60. *Diagnosis:* Typhus fever. Mild parotitis in convalescence.

Clinical Notes

May 19. Physical Examination: The patient is too dull and confused to reply to questions rationally. The face is much tanned and the cheeks are slightly flushed. The pupils are equal and of normal size. The tongue shows a brownish coat. The throat is negative and the mucous membranes are free from spots.

The Eruption is scanty on the neck and hands and indefinite on the legs. The chest, flanks, abdomen, back, and arms are profusely covered with small purplish-brown spots. There are a few minute purple spots on the forearms and elsewhere. Evidently they are flea bites.

Heart: The pulmonic second-sound is accentuated and occasionally reduplicated. It is louder than the aortic second-sound. The second-sound at the apex is accentuated. The first-sound is faint, and blurred by a soft, systolic murmur which is best heard in the pulmonic area. Blood-pressure, 90/S.–50/D.

The Lungs are negative.

The Abdomen is flat, soft, and not tender. The liver and spleen are not palpable and the splenic dulness is not increased.

The neck is very slightly stiff, but the neck muscles are not sensitive. Kernig's sign is present, slight in degree. The test causes no pain. The muscles are not sensitive to pressure.

Treatment consisted of routine measures without drugs.

May 22. The right cheek began to swell yesterday in the region of the parotid gland. The temperature rose a little. Cold compresses were applied locally.

June 2. The tenderness and swelling of the parotid have never been great. The swelling diminished markedly two days ago after poulticing. Now there is no tenderness and no pain. The swelling which remains is slight, and very hard. There is slight, irregular fever, but the patient looks and feels well.

June 10. Discharged well except for slight, hard swelling of the parotid gland.

SERIES NUMBER 61. *Diagnosis:* Typhus fever; severe case, eruption peculiar, delirium violent.

Clinical Notes

May 20. Patient was admitted yesterday.

Physical Examination: The patient is drowsy but rational. The entire face is flushed, especially the cheeks and ears. The pupils are small, equal, and react to light. The conjunctivae are red. The tongue shows a brownish coat, the throat is slightly red, and the mucous membranes are free from spots.

Eruption: The lower part of the neck, the chest, and the arms show many rose-pink macules which disappear entirely on pressure and which are not elevated. There are a few macules on the abdomen, legs, and feet. The flanks show a few papules which are redder in color than the macules and which do not disappear entirely on pressure. The face and hands are free from spots.

Extensive pink mottling is seen on the back and there are blotches of irregular outline and considerable size scattered over the trunk. They resemble pityriasis rosea.

Heart: Dulness is normal in extent. The sounds are of good quality except the aortic second-sound which is rather faint. The pulse is of good volume and tension.

The Lungs are negative.

The Abdomen is very soft and tympanitic. It shows considerable general tenderness without spasm. The spleen is palpable on deep breathing and the splenic dulness is increased.

The neck muscles are very sensitive to pressure and the neck is stiff. The hamstring and calf muscles are very sensitive, and the thigh muscle in front is less so, and the biceps is still less sensitive. Kernig's sign is positive but slight in degree. The test causes pain. Routine treatment prescribed.

May 21. White count, 8600.

May 26. The patient has been delirious since admission. At first he would get up and try to leave the ward. The night before last the delirium became so violent that the patient had to be tied in bed. This morning he was quiet but mentally confused.

The face has become several shades *darker in color*. The conjunctivae are still deeply injected. The patient lies on his back and dozes with eyes half open.

Heart: The pulmonic second-sound is accentuated and louder than the aortic second-sound. The first-sound is of good quality. The pulse is of good volume. Blood-pressure, 95/S.–65/D. Haemoglobin (Tallquist), 75 per cent.

May 27. The pupils remain contracted.

June 12. This patient has been very ill and has gained strength slowly. He has been drowsy and lethargic but now looks decidedly better. For several days his bed was put out of doors but for the past three days he has been able to walk out. Today he returned complaining of headache. The weather has been very hot.

Three days ago white spots, like thrush, appeared in the throat. They are clearing up now.

Examination of the heart shows the first-sound short but louder than the second-sound and the pulmonic second-sound louder than the aortic second-sound which is faint. Blood-pressure, 125/S.–60/D.

The skin and mucous membranes are pale. Haemoglobin (Tallquist), 90 per cent.

An iron tonic and small doses of digitalis were prescribed.

June 18. The patient is rather pale and lethargic. His condition is otherwise satisfactory. He will be discharged tomorrow.

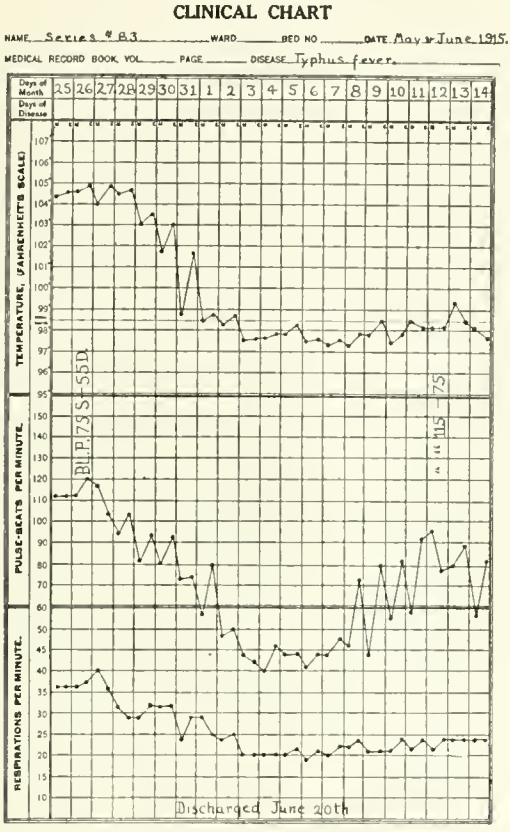
Series Number 83. *Diagnosis:* Typhus fever. Bradycardia; heartblock (?). Digitalis used.

Clinical Notes

May 25. The patient says he was ill for a week before admission.

Physical Examination: The patient is mentally clear and alert. The tongue shows a brownish coat.

The Heart Action is regular, the sounds at the base are of good quality but at the apex they are faint. The pulmonic second-sound is accentuated and louder than the aortic second-sound. The pulse is small and rapid.



SERIES NUMBER 83. Typhus fever. Bradycardia, heart-block (?). Digitalis used

The Lungs are negative.

The Abdomen is negative. The spleen is not palpable but splenic dulness is increased.

The neck is not stiff and Kernig's sign is absent. The knee-jerks are sluggish. Digitalis was prescribed.

May 26. (Morning.) The soft palate and the pharynx are red. On the palate is a single minute red spot. The entire face is flushed and especially the cheeks and ears. The conjunctivae are much injected. The pupils are small.

There are a few spots on the neck. The chest, the back, the abdomen, and the backs of the feet and hands are profusely sprinkled with spots.

The neck is not stiff or sensitive. There is a slight bilateral Kernig's sign more definite on the right. Performance of the test causes pain in the hamstring muscles. They are slightly sensitive to pressure.

The patient is rational but rather dull.

The pulse has been of poor quality since admission. Blood-pressure, 75 S.–55 D.

The condition of the patient is otherwise excellent. Haemoglobin (Tallquist), 90 per cent. The urine is high colored.

Increased ingestion of water was prescribed and a small dose of strychnin every four hours.

May 26. (Afternoon.) Every third or fourth heart beat is skipped. The sounds are loud. The pulse is now of good volume and tension. Digitalis omitted. The doses taken since admission have not been large.

May 27. The cardiac irregularity is less pronounced but the pulse rate continues to fall.

June 12. Haemoglobin (Tallquist), 90 per cent.

The heart action is rapid again and regular. The pulmonic second-sound is louder than the aortic second-sound. The first-sound is louder than the second-sound at the apex. In the aortic region a short, scratchy systolic murmur resembling a pericardial friction rub is heard. Blood-pressure, 115 S.–75/D. Digitalis was prescribed again.

June 13. Because the pulse rate fell markedly and irregularity recurred the digitalis was omitted this morning. In the afternoon the pulse was again more rapid and there was no arrhythmia. The patient had been walking about the ward a little. Blood-pressure, 120/S.–80/D.

June 20. Discharged in good condition.

Series Number 92. *Diagnosis:* Typhus fever in an old man; mild; premature systoles.

Clinical Notes

June 11. Nationality Turkish, age 60.

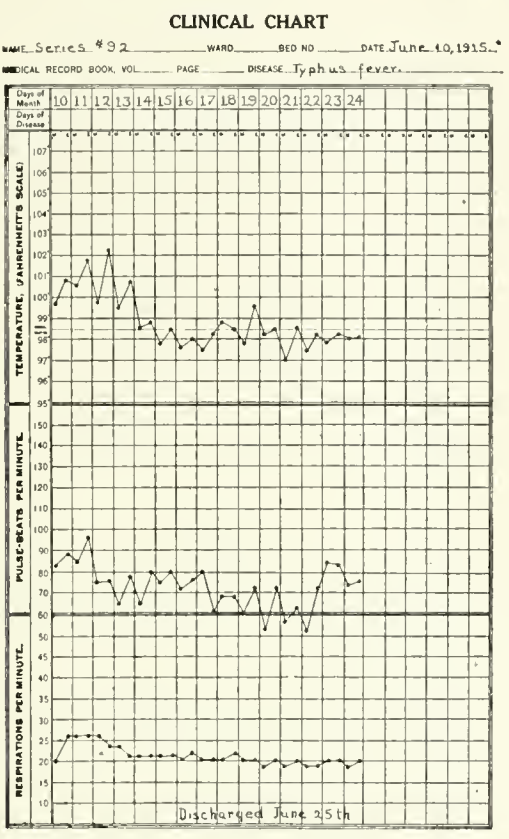
Present Illness: Admitted yesterday having been "sick eight days." The patient was incontinent last night and is so today. He was stuporous yesterday but is brighter today. He is taking nourishment fairly well in small quantities. There is no cough or expectoration.

Physical Examination: The patient is very drowsy, but when aroused replies intelligently. He lies most of the time with the eyes half closed and the mouth open, grunts occasionally but breathes easily and does not cough. The skin is rough and dry. The body is well developed but emaciated and dried up.

The face is very brown but markedly flushed. The hyperaemia extends over the forehead and neck and down on to the upper part of the sternum.

The conjunctivae are moderately injected. The pupils are equal, of moderate size, and react to light. The tongue shows a heavy brownish coat. It is dry and fissured. The throat is red and sticky mucus adheres to it.

Eruption: The chest, arms, abdomen, and back show many spots midway between the pink and purple stages. The spots are macular, and



Series Number 92. Typhus fever in an old man; mild; premature systoles

they nearly disappear on pressure. The legs, backs of the forearms, hands and feet and face are free from spots.

The heart's action is regular. The aortic second-sound is slightly accentuated and the pulmonic second-sound is faint. The second-sound at the apex is accentuated and the first-sound has a valvular quality. Blood-pressure, 85/S.-65/D.

The Lungs are negative.

The Abdomen is soft and is not sensitive. Peristalsis is visible. The liver and spleen are not palpable and splenic dulness is not increased.

The neck cannot be bent forward at all, but rotation is free. There is no sensitiveness of the neck muscles. The Kernig's sign is present and this test causes pain. The knee-jerks are present, but very sluggish. The abdominal and plantar reflexes are present and lively. Haemoglobin (Tallquist), 85 per cent.

Prescribed brandy, 15.0 c.c. and digitalis, 0.6 gm. every four hours.

June 15. The heart sounds are of fair quality. Single or double premature systoles are heard occasionally. The pulse is of good volume and fair tension. Blood-pressure, 90/S.–55/D.

The eruption is fading. Only a few pale, brown spots remain.

The patient sleeps a great deal. He has always taken nourishment well and seems to be improving. He has given no cause for alarm. Constipation is very obstinate.

June 18. The aortic second-sound is faint, the pulmonic second-sound is of fair quality, and the first-sound is short. The second-sound at the apex is good. Blood-pressure, 90/S.–55/D.

June 25. Discharged in good condition.

SERIES NUMBER 93. *Diagnosis:* Typhus fever; bronchopneumonia; dry pleurisy.

Clinical Notes

Present Illness: Serbian, age 40, admitted to the wards of a colleague June 5 and transferred to the writer on June 8. The patient is said to have been ill eight days before admission and to have had an eruption which first appeared nine days ago.

June 11. Physical Examination: The patient is drowsy, but easily aroused and is then apprehensive because every movement which involves the shoulder causes pain. He appears to be rational. The respiration is rapid and shallow and the nostrils move.

The face is very brown and there is a slight malar flush. The pupils are equal, of medium size, and react to light. The tongue shows a heavy brownish coat. The throat is reddish and there is sticky mucus adherent. The skin is dry and rough.

The eruption is profuse, purple, blotchy, and is beginning to turn brown. It is abundant on the chest, abdomen, and back, and less so on the arms and thighs. The forearms, lower legs, feet, and hands are free from it or nearly so.

The heart action is very rapid but regular. The aortic second-sound is louder than the pulmonic second-sound. The second-sound at the apex is accentuated. The first-sound is short and has a valvular quality. The pulse is small and of low tension. Blood-pressure, 80/S.–60/D.

The Lungs are negative.

The Abdomen is soft and seems to be acutely sensitive all over. Pressure anywhere on the abdomen causes the patient's face to show signs of pain. The spleen is not palpable and the splenic dulness is not increased.

The neck is very stiff and the neck muscles are sensitive. The head rotates freely but cannot be bent forward. The Kernig's sign is well marked. The muscles of the thighs and calves appear to be very sensitive to pressure.

For three days the patient has been receiving 0.6 gm. of digitalis and 15.0 c.c. of brandy every four hours. The night before last salt solution by rectum every six hours was prescribed. At first it was all retained, but now some of it is being lost. The bowels became incontinent yesterday.

The patient coughs much but expels the secretion with great difficulty because he is very weak and the sputum is extremely viscid. It frequently causes a rattle in the throat.

The nourishment was well taken until last night.

The pulse is more rapid and becomes bad whenever the patient is disturbed. The blood-pressure at 11.30 A.M. was 75/S.–65/D. The aortic second-sound was of fair quality. The pulmonic second-sound and the first-sound were faint. At 5 P.M. the blood-pressure was 80/S.–65/D., and the heart sounds as before. The pulse was very weak. The area of heart dulness was less than normal. (Front of chest hyperresonant.)

The Lungs were practically clear and the breathing easy but rapid. At 5.30, about 480 c.c. of salt solution were administered intravenously. During the injection the pulse improved in quality, and the heart sounds became stronger; the blood-pressure after the injection was 83/S.–60/D. Half an hour before the injection the pulse rate was 140. Immediately after the injection it was varied between 132 and 136. About 15 or 20 minutes after the infusion the patient had a prolonged and severe rigor during which his color became dusky and the pulse scarcely perceptible. The rigor lasted about 15 minutes and the patient's condition afterward was much the same as before the infusion. Haemoglobin (Tallquist), 100 per cent.

June 13. The temperature is falling and the condition has improved.

June 15. Yesterday afternoon the patient's condition again became critical. He was given tea last night. He rallied again this morning and now seems decidedly better. The eruption is fading. Blood-pressure at noon, 90/S.–75/D.

For the past three days he has been taking nourishment poorly.

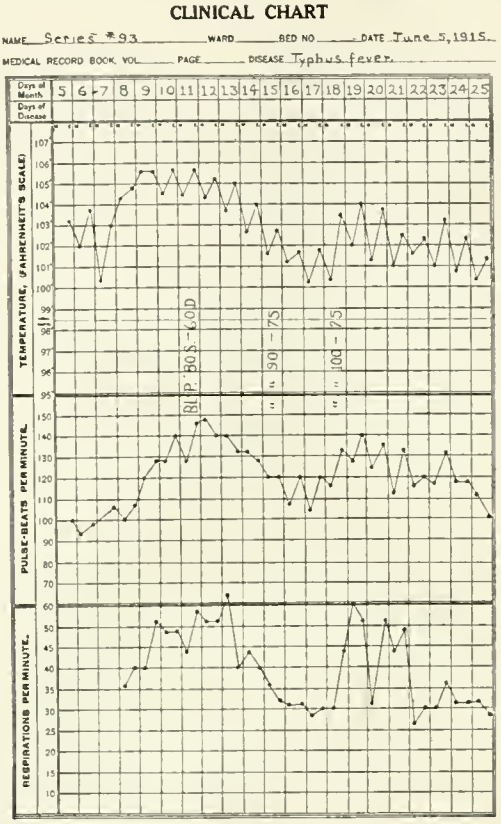
June 17. There has been severe diarrhoea for several days. Opium and an astringent mixture were given to check it.

Last night the circulatory condition was unsatisfactory. Salt solution, about 360 c.c., were given intravenously. There was no rigor. The pulse is of fair quality this morning.

There is a good deal of cough and a considerable quantity of thick, whitish expectoration. Nourishment is taken better this morning.

Urine: Normal color, sp. gr. 1016, no albumen, no bile.

The pulse in the afternoon became poor in quality. The rate was 104. Salt solution was prepared in the most careful way, the temperature care-



Series Number 93. Typhus fever, severe; bronchopneumonia, dry pleurisy

fully regulated, and about 480 c.c. were given intravenously. The patient had a severe rigor after it. He was then given a small dose of morphin subcutaneously and slept well.

June 18. Blood-pressure this morning 100/S.–75/D.

June 24. Since the 19th there has been a gradual fall of temperature and slow but steady improvement in the patient's condition.

About June 20 a friction-rub was heard at the right base. Yesterday the lungs were negative except for a few râles at the bases.

The patient occasionally expectorates thick lumps of whitish mucus with great difficulty on account of weakness. He succeeds only with help and encouragement from the nurse.

The sputum looks as if it came from the nasopharynx, but the nurse feels sure that it is raised from the chest. Microscopical examination of the sputum shows no tubercle bacilli, but many pneumococci and various other bacteria are present. There are a few spirochaetae and influenza-like bacilli and a very few pus cells. The sputum has had a foul odor occasionally.

July. When last seen the patient was convalescent and had no cough. But for the remarkably assiduous care of the nurse the pulmonary complications would almost certainly have proved fatal.

The diagnosis of bronchopneumonia in this case was based on severe pulmonary symptoms combined with a secondary rise of temperature.

TYPHUS FEVER, FATAL CASES. AUTOPSY

AUTOPSY NUMBER 4. Patient of Dr. ——.

Diagnosis: Typhus fever, pulmonary oedema, bronchitis.

Died, probably, during the stage of nervous depression.

Apparent Cause of Death: Acute myocardial weakness, chronic nephritis, and (?) early pneumonia.

Clinical Notes

Rapid breathing, etc., before death suggested pneumonia.

Autopsy Findings

Postmortem performed 24 hours after death. Body emaciated and livid.

Heart: Not dilated, muscle pale, rather flabby. Mitral orifice slightly large. Valves natural. An ante-mortem (?) thrombus was found in the left ventricle.

Lungs: Many pleural adhesions, bilaterally distributed, some old, others more recent. On the pleural surface at the right apex a fresh haemorrhage was found. The *right upper lobe* was *oedematous* and *congested.* The left lung was deeply congested throughout. Even the apex was oedematous.

In the bronchioles of the left lower lobe purulent exudate was found.

Liver: Pale and slightly fatty.

Spleen: Large, dark red, confluent.

Kidneys: Slightly diminished in size, capsules firmly adherent. Surface of section pale, cortex and medulla not markedly abnormal but slightly congested.

Specimens: Left kidney, right ventricle, lower lobe of left lung, spleen, and liver.

AUTOPSY NUMBER 5. (A I.) Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the postfebrile stage.

Apparent Cause of Death: Gradual exhaustion and cardiac weakness.

Clinical Notes

The day before he died the patient was semicomatose, delirious, and prostrated. The pulse was of the Corrigan type and *a diastolic murmur was*

heard near the fourth left costal cartilage. About 360 c.c. of salt solution was given under the pectoral muscle in the afternoon. The next morning the patient's condition was worse, but the *force* and *volume* of the *pulse* was *good.* Half an hour later he died. The patient had passed through the febrile period of typhus before death.

Autopsy Findings

Body of young man, extremely emaciated.

Heart: Slightly dilated; muscle flabby. Slight old thickening of mitral valve. *Aortic valves normal.*

Passive Congestion of all organs.

Stomach: Extremely distended with air.

Specimens: Heart muscle, liver, spleen, kidney.

This case called to mind one in which Dr. Smith saw tetany for several days, followed by recovery. Was the tetany due to gastric dilatation?

AUTOPSY NUMBER 6. (A II.) Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the stage of nervous depression or later.

Apparent Cause of Death: Gradual exhaustion. Old mitral stenosis found.

Clinical Notes

Age 45. Died late in disease.

Autopsy Findings

The body is emaciated.

Heart: Left ventricle considerably hypertrophied and firmly contracted. Right ventricle dilated, muscle firm. Mitral orifice stenosed, cresentic in shape, admits one finger with difficulty. Other valves natural.

Lungs: Many dense fibrous adhesions of the pleura. A nodule at the left apex, probably tuberculous; old scars at right apex.

Spleen: Large and soft, surface of section pale.

Liver: Large, deeply congested, slight fatty degeneration.

Kidneys: Appear normal.

Specimens: Left ventricle, spleen, liver, kidney.

AUTOPSY NUMBER 7. Patient of Dr. Holmes.

Diagnosis: Typhus fever, lobar pneumonia.

Death during the stage of nervous depression or later.

Apparent Cause of Death: Lobar pneumonia as a complication.

Clinical Notes

On admission, April 26, patient was said to have been sick eight days, but the presence of a scanty, old rash made it probable that he had been ill longer than the time stated.

The temperature dropped to 101° on the second day after admission and continued at about that level, with the pulse at from 90 to 100, and the respiration at from 24 to 26 until the patient died on May 5.

Autopsy Findings

Postmortem performed four hours after death.

Body covered with small petechial spots.

Heart: Muscle firm and dark in color. No dilatation. Valves not remarkable.

The Aorta showed slight atheroma of the first part of the arch.

Lungs: All except the apex of the upper lobe of the left lung was consolidated as was also the right lower lobe. The process was evidently recent.

Liver: Deeply congested.

Spleen: Large, soft, dark red.

Kidneys: Marked passive congestion.

Specimens: Left ventricle, kidney, heart. (No. A.)

AUTOPSY NUMBER 8. Patient of Dr. ——.

Diagnosis: Typhus fever.

Died during the postfebrile stage.

Apparent Cause of Death: Gradual exhaustion with circulatory weakness, probably vascular in origin.

Clinical Notes

Toward the end of defervescence the patient developed signs of circulatory weakness which increased in spite of medication until he died a week later. Salt solution was not administered.

Autopsy Findings

Postmortem performed sixteen hours after death.

Extreme emaciation, muscles very dry.

Heart: Right ventricle not dilated. Left ventricle firmly contracted. Valves appear normal.

Lungs: Pale, anterior borders emphysematous, posterior margins congested. There is a *recent infarct,* deep red in color, 2.5 to 4 cm. in diameter at the anterior margin of the right lower lobe.

Liver: Large, passively congested.

Spleen: Small, dark, firm.
Kidneys: Congested, not otherwise remarkable.
Specimens: Lung infarct, liver, kidney, heart. (No. B.)

AUTOPSY NUMBER 9. (C.) Patient of Dr. Smith.
Diagnosis: Typhus fever.
Died during late stage of nervous excitement or early in that of nervous depression.
Apparent Cause of Death: Acute exhaustion probably with terminal circulatory weakness. Slight old mitral stenosis.

Clinical Notes

Age 53. The patient was violently delirious, especially at night, for several days before death. The delirium prevented sleep and continued every night until the patient became exhausted. Then he would be quieter for a time. When active he presented the appearance of delirium tremens, sat up in bed grinding his teeth, looked about wildly, and rolled his eyes. Apparently, he had terrifying delusions. Mucus collected rapidly in the throat and required frequent attention. The pulse at first was rapid and of the bounding type. The breathing was very rapid.

The afternoon before death, faint, distant, bronchial breathing was heard at the left base behind. No dulness was found. The breathing was rapid and labored, and the general picture was that of pneumonia in an alcoholic individual.

Autopsy Findings

Body not emaciated. Traces of rash persist.
Heart Muscle: Soft and dark in color. Left ventricle in systolic contraction. Right ventricle slightly dilated. Mitral orifice admits two fingers with difficulty. Valves slightly shrunken and thickened. No evidence of recent damage. Other valves natural. Great vessels engorged with blood.
Lungs: Bloody exudate in left lower lobe representing perhaps the first stage of pneumonic consolidation. Both lungs emphysematous in front. Right lung not otherwise remarkable.
Liver and *Kidneys:* Markedly congested.
Spleen: Large, dark, confluent.
Specimens: Liver, spleen, kidney, heart. (No. C.)

AUTOPSY NUMBER 10. (C.) Patient of Dr. Holmes.
Diagnosis: Typhus fever.
Died during the postfebrile period.
Apparent Cause of Death: Gradual exhaustion.

Clinical Notes

Age 30. Ill about five weeks.

Autopsy Findings

Postmortem performed twelve hours after death.

Considerable emaciation. No visible eruption. Subcutaneous fat small in amount.

Heart Muscle: Pale. Otherwise normal in appearance.

Aorta: Shows a trace of atheroma.

Lungs: Bilateral pleural adhesions, apparently rather recent. Hypostatic congestion at bases, greater on the left than on the right.

Liver: Few old adhesions to surrounding structures. Organ enlarged but not cirrhotic.

Spleen: Large, soft, rather pale.

Kidneys: Of normal size, capsules adherent in places, moderately congested. Otherwise not remarkable.

Specimens: Liver, spleen, kidney.

AUTOPSY NUMBER 12. (S. No. 45.) Patient of Dr. Holmes.
Diagnosis: Typhus fever.
Death during the stage of nervous depression.
Apparent Cause of Death: Acute myocardial weakness.

Clinical Notes

Serbian soldier, admitted May 7.

May 8. White count, 12,000.

May 9. (Examination by writer.) On cheeks, nose, and chin are large blotches of haemorrhage beneath the epidermis. They are sharply defined and dark red in color. Traumatic excoriations on back. The patient is said to have had a fight in barracks.

The trunk, back, arms, and legs show an abundant, macular, purplish eruption. The patient lies on the back, comatose, snoring, and can be aroused with difficulty. He breathes through the mouth rapidly and deeply.

Heart Sounds of poor quality, action rapid, no murmurs.

The pulse is soft and of fair volume, but irregular in force. Blood-pressure, 90/S.–65/D.

Lungs: Clear in front and at sides, back not examined.

Blood: Haemoglobin (Tallquist), 100 per cent ++; by Sahli, 115 per cent. Red count, 5,000,000.

May 11. Coma increased and patient died.

Autopsy Findings

May 12. Body well nourished.

Heart: Both ventricles much dilated, flabby, and full of blood. Valves not remarkable.

Lungs: Showed a few old adhesions.

Intestines: Showed a few old adhesions. The colon was enormously distended with gas.

Kidneys: There seemed to be a slight excess of connective tissue and some fatty infiltration.

Passive Congestion of all organs.

Brain: Very oedematous. No gross lesion found.

Specimens: Whole heart and pieces of organs.

AUTOPSY NUMBER 13. (S. No. 50.) Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the postfebrile stage.

Apparent Cause of Death: Gradual exhaustion, myocardial weakness.

Clinical Notes

The patient had a profuse eruption at the time of admission. Defervescence by lysis followed, the temperature remained normal for seven days and during this time the patient was apparently improving slowly. Then fever recurred without apparent cause and four days later the patient died with "dyspnoea and distress" which came on during the night.

Corneal ulceration appeared at about the end of the febrile period.

Autopsy Findings

Body of man past middle age, extremely emaciated. Muscles much wasted and very dry, but plenty of blood in veins.

Heart Muscle: Flabby. Right ventricle moderately dilated. Valves natural.

Lungs: Bilateral pleural adhesions, some old, others more recent. Slight congestion of bases.

Liver: Engorged with blood. Slight fatty degeneration.

Spleen: Small, dark, firm.

Kidneys: Apparently there is some fatty infiltration without evidence of interstitial change.

Specimens: Pieces of organs.

AUTOPSY NUMBER 14. (S. No. 51.) Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the postfebrile stage.

Apparent Cause of Death: Gradual exhaustion, myocardial weakness.

Clinical Notes

Ill for a long time. Temperature reached normal nine days after admission and remained there except for slight recurrences until the death of the patient *nineteen days* later.

Autopsy Findings

Body of man past middle age, extremely emaciated. Muscles extremely wasted. Abdominal wall lies against spinal column.

Heart Muscle: Pale, flabby, no dilatation, valves natural.

Lungs: Many pleural adhesions which appear to be of recent formation. One small pleural fibroma, perhaps tuberculous. No fluid in pleural cavities, *no congestion,* and no consolidation.

Larynx: Shows slight chronic swelling of mucosa. Vocal cords normal.

Thyroid Gland: Not remarkable.

Liver: Slight passive congestion.

Spleen: Of normal size, soft.

Kidneys: Capsule strips easily. There is slight interstitial fibrosis and moderate passive congestion.

Specmens: Thyroid, liver, spleen, kidney, lung.

AUTOPSY NUMBER 16. (S. No. 58.) Patient of Dr. ——.

Diagnosis: Typhus fever, acute and chronic, nephritis, enlarged thymus.

Died during the last stage of the febrile period or immediately after it.

Apparent Cause of Death: Uraemia as a complication.

Clinical Notes

Admitted May 16, age 30. Eruption typical. The temperature dropped by rapid lysis. The urine was scanty. The patient died in a convulsion.

May 17. Haemoglobin (Sahli), 115 per cent. Red count, 5,000,000. White count, 15,000.

Autopsy Findings

May 19. Postmortem performed three hours after death. Body slightly emaciated, eruption visible.

Heart Muscle: Firmly contracted, wall of left ventricle seems to be a little hypertrophied. A few small patches of atheroma in the sinuses of Valsalva. No other abnormalities seen.

Lungs: Pleural cavities nearly obliterated by adhesions. Some of those on the right appear to be recent, the others are old. Posterior margins of lungs congested.

Thymus Gland: Larger than normal. Adhesions between sternum and mediastinal contents.

Abdominal Cavity: Shows many old adhesions of omentum to abdominal wall and to intestines.

Liver: Thickly covered with old fibrous adhesions.

Spleen: Buried in a mass of old adhesions, much enlarged, and very soft.

Kidneys: Both much enlarged. Surface of section gritty, pale, and grayish in color. Appearance suggests acute process superimposed on a chronic nephritis.

Specimens: Left ventricle, liver, spleen, kidney.

AUTOPSY NUMBER 17. (S. No. 53.) Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Coma, bronchitis, and pulmonary congestion.

Clinical Notes

Admitted May 14.

May 15. (Examination and notes by writer.) Patient lies on back, eyes closed, knees drawn up and apart, breathing rapid and shallow, but without effort; wakes frequently and looks about anxiously as if having bad dreams. There is a slight rattle in the throat and the patient groans from time to time. The face is dark brown and cyanotic as are also the lips and ears. The conjunctivae are injected. The pupils are equal and unusually large.

The Eruption is chiefly macular but some of the spots are elevated to the touch. The color is brownish purple. The trunk and arms are so profusely covered by the rash that no normal skin can be seen. There are many spots on the legs, and a few on the backs of the hands and feet. There are a few circular, red spots of uniform size and smaller than the head of a pin. They are old flea bites.

The Heart Action is rapid, and the sounds are of fair quality, but partly obscured by râles. The first-sound is short. The pulse is regular, of good volume, and diminished tension.

Lungs: Chest of barrel type, hyperresonant in front. There are many medium râles in front, and coarser râles behind, but no bronchial breathing or dulness.

Abdomen: Shows slight general sensitiveness. The bladder is distended to the umbilicus. Urine and faeces are passed involuntarily.

The Knee-jerks are present. There is a slight Kernig's sign. The muscles of the calves and thighs are not sensitive. The neck is very slightly stiff.

Haemoglobin, 100 per cent or more. The color does not correspond well with that of the Tallquist scale.

Blood-pressure, about 95 S.–80 D., but variable. Some systolic sounds are heard at a pressure of 100 mm. showing variation in force of the pulse. The variation seemed to be dependent on the phase of the respiration.

May 17. Blood-pressure, 100 S.–85 D. Breathing easier, cyanosis less, no rattle in throat, râles heard only at the backs. Mildly delirious but brighter. Haemoglobin (Sahli), 130 per cent. Red count, 5,600,000. White count, 4300.

May 21. Since last note the patient has alternately improved and relapsed. He has been constantly more or less delirious. Yesterday he became comatose. The pulse today is smaller and weaker than it was. The pupils are very small. The patient died at 10 P.M.

Autopsy Findings

Postmortem performed twelve hours after death.

Body strongly developed and well nourished, apparent age 40 years. Extreme lividity.

Heart: Normal in size, in systolic contraction, neither ventricle dilated, muscle firm. Otherwise natural. There is a very small patch of atheroma on the aorta.

Lungs: Congestion slight in right lung, marked in the left. No consolidation. The bronchi contain thick, blood-stained mucus. Mucous membrane of bronchi red and swollen.

Liver: Moderately enlarged and congested.

Spleen: Adherent to the abdominal wall in the flank, twice the normal size, soft.

Kidneys: Appear normal.

Urine from bladder contains much albumen, some pus, a few red blood-cells and casts.

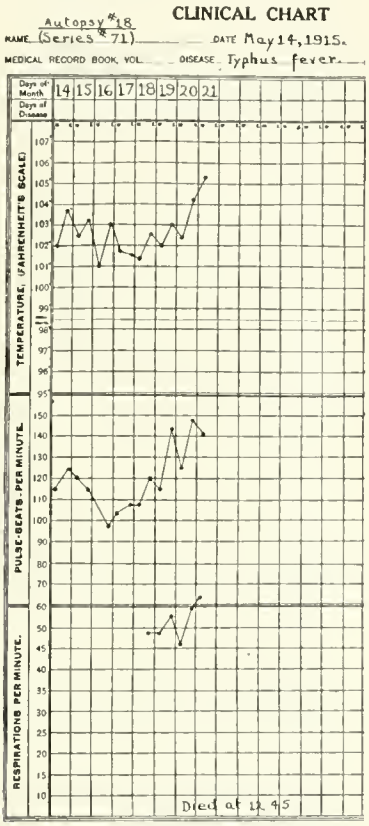
Specimens: Whole heart, liver, spleen, and kidney.

AUTOPSY NUMBER 18. (S. No. 71.) Patient of writer.
Diagnosis: Typhus fever.
Died during the stage of nervous depression.
Apparent Cause of Death: Coma, beginning pneumonia (?).

Clinical Notes

May 19. Patient transferred today from another ward, feeble and mildly delirious. There was a profuse purple eruption when he was admitted to hospital on May 14.

Heart Sounds: Obscured by râles. Pulse good.



AUTOPSY NUMBER 18. Typhus fever. Coma, (?) beginning pneumonia

Lungs: At the right base there is dulness with diminished breath sounds and râles. At the left base there are râles, and at the angle of the left scapula distant bronchial breathing is heard.

May 20. The patient takes fluid badly but excretes it well. He coughs occasionally, but lacks strength to spit. The respiration is very rapid, and suggests pneumonia. The arms, and especially the hands, twitch constantly. The patient sweats profusely and is comatose and incontinent.

May 21. Died this morning.

Autopsy Findings

May 21. Body of man of middle age, well nourished. The eruption has faded.

Heart: Several milk patches on visceral pericardium. The heart is rather small and contracted. The muscle appears normal and the valves natural. There are a few small patches of atheroma on the aorta. The coronary orifices are normal.

Lungs: No pleural adhesions. Near the apex of the right lower lobe there is a patch of congestion about three inches in diameter. There is no consolidation. The bases are not congested, and the lungs, otherwise, appear normal.

Abdomen: Colon much distended with gas. A mass of old fibrous adhesions surrounds the spleen.

Spleen: Shows thick patches of fibrous tissue on its surface.

Liver: Definitely but slightly cirrhotic, and slightly enlarged.

Kidneys: Congested, not otherwise remarkable.

Specimens: Whole heart and pieces of organs.

Autopsy Number 19. (S. No. 81.) Patient of Dr. Smith and of writer.

Diagnosis: Post-typhus parotitis and cellulitis with septicaemia.

Died during the stage of nervous depression.

Apparent Cause of Death: Parotitis and septicaemia.

Clinical Notes

Austrian soldier. Transferred from another ward in the later stages of typhus fever. Previously, he had a definite rash which has now disappeared.

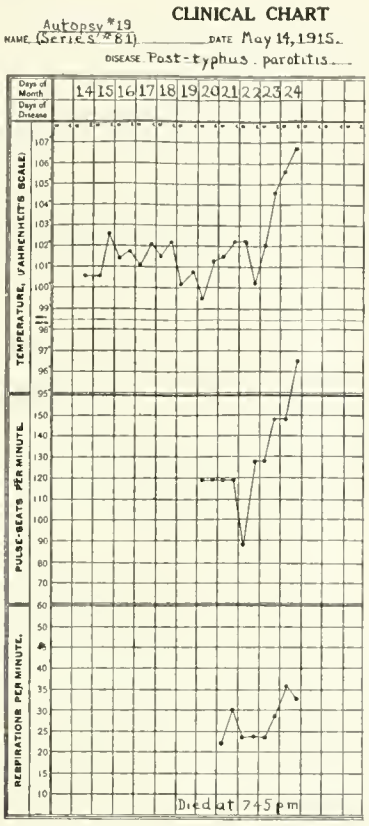
May 19. The patient is extremely thin. Both cheeks are much swollen, hard, and moderately sensitive, causing much pain and making swallowing very difficult.

May 21. Increased fever. Fluctuation can be definitely felt on the right cheek in front of the ear. An incision was made by Dr. Smith under chloroform anaesthesia and several ounces of thick pus were evacuated. White count, 9100.

May 22. The temperature remains high and the pulse rapid. There is little discharge from the incision on the right and the swelling has increased. Therefore another incision was made at the angle of the jaw on the same side but very little pus was found. A third incision was then made on the left side below the ear and 15 to 30 c.c. of thick pus were evacuated.

May 23. Today the skin and conjunctivae showed slight jaundice. The patient has been practically without nourishment for several days. A little was given through a nasal tube. Urine, sp. gr. 1018, bile present.

May 24. The swelling under the chin which began a few days ago has increased in spite of the incisions over both parotids. The temperature is



Autopsy Number 19. Typhus fever. Parotitis and septicaemia

very high and breathing is difficult. Under local anaesthesia Dr. Smith made a deep incision under the chin but the amount of pus evacuated was small. The tissue was firm and oedematous. The patient died at 7.45 P.M.

Autopsy Findings

Postmortem performed thirteen hours after death.

Body of man of about 35 years of age. Extremely emaciated.

Heart: Slight excess of clear yellowish fluid in the pericardial sack. The organ is of normal size, and firmly contracted. The muscle is pale, and

rather soft. On one curtain of the tricuspid valve and on the wall of the heart above it are patches of oedema with a little extravasation of blood. The valves appear otherwise normal.

Lungs: Appear normal. There is little if any oedema.

Abdomen: Intestines moderately distended with gas.

Liver: Rather small. The surface of section is shiny and stained with bile. The markings are indistinct.

Spleen: Much enlarged and very soft.

Kidneys: The left kidney is about twice the normal size. The capsule strips easily. The surface of section shows pale streaks in the cortical region and the markings there are indistinct.

The right kidney is about one-half the normal size, and is moderately congested, but otherwise normal in appearance.

Larynx: Mucous membrane slightly swollen and injected but not oedematous.

Specimens: Pieces of organs.

Autopsy Number 20. (S. No. 84.) Patient of writer.

Diagnosis: Typhus fever.

Died during the state of defervescence.

Apparent Cause of Death: Chronic myocardial degeneration.

Clinical Notes

May 26. The patient is an old man sent yesterday from another ward. He is well developed, but poorly nourished. He is mentally clear.

The face is not flushed. The conjunctivae are slightly injected. The pupils are equal and of normal size. The tongue shows a slight, white coat. The throat is negative except for shreds of thick mucus adherent to it.

The Eruption is small, macular, and purplish-pink. Most of the spots disappear completely on pressure. The spots are best seen on the inner surfaces of the arms and wrists and on the sides of the chest where they are numerous. There are few or none in other parts.

The Heart Action is rapid and regular. The second-sounds are of good quality. The first-sound is short and valvular, and the pulse small and weak. The arteries are palpable. Blood-pressure, 75/S.–60/D.

The Abdomen is flat, and shows slight general sensitiveness. The spleen is not palpable and splenic dulness is not increased.

The knee-jerks are present. There is no sensitiveness of the leg muscles, and no Kernig's sign. The neck is not stiff. Haemoglobin, 85 per cent.

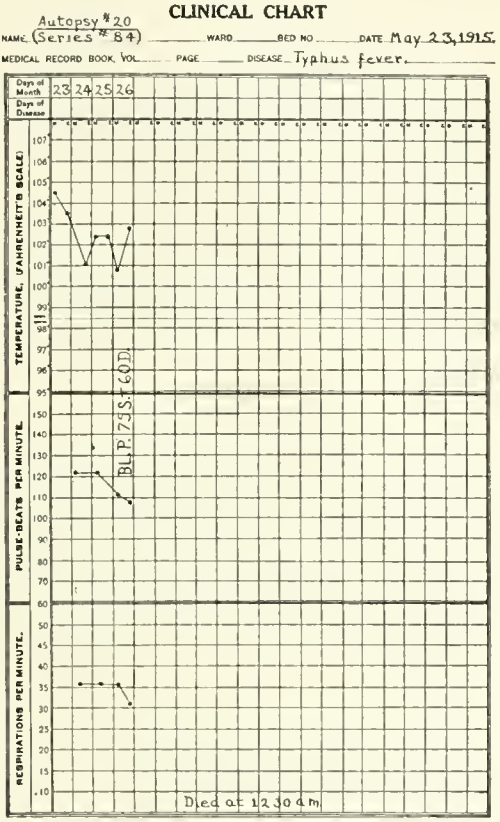
Date (?). The patient has vomited a little. He dislikes liquids, but eats bread.

At midnight the patient was given something to drink and seemed all right. At 12.30 A.M. when the nurse returned to the ward to get something the patient made a sudden motion and died immediately.

Autopsy Findings

Postmortem performed ten hours after death. Body emaciated.

Heart: Normal in size and not dilated. Muscle brown and flabby. Cardiac vessels not tortuous. Slight old thickening of the mitral valve,



AUTOPSY NUMBER 20. Typhus fever. Chronic myocardial degeneration

the orifice of which admits two fingers. The other valves, the aorta, and the coronary arteries are natural.

Lungs: Many pleural adhesions on left side. The back of the left lung and *especially the apex of the lower lobe* is dark in color, and on section a haemorrhagic fluid exudates. The lung feels leathery. The apex of the left lung

remains distended and feels like a cyst. On cutting it a clear fluid exudates. On the right side there are fewer adhesions than on the left and the lung is less congested than the left.

Abdomen: Intestines moderately distended but otherwise normal in appearance.

Liver: Of normal size. Surface of section pale brown in color and greasy. It is pitted here and there and shows yellowish spots. (Slight fibrosis and fatty changes.)

Spleen: Firmly adherent to surrounding structures. Capsule nearly covered with patches of old fibrous tissue. Organ much enlarged. Pulp almost fluid.

Kidneys: The left is large, and its markings are vague and confused by whitish streaks and spots. The right is smaller than the left, and is similarly abnormal in appearance but to a less degree.

Specimens: Whole heart and pieces of organs.

Autopsy Number 21. Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Coma and diarrhoea with terminal circulatory collapse.

Clinical Notes

On admission the patient had a typical and very profuse rash. He died three days later. The nurse said that the patient was comatose from the time of admission, that the throat was covered with dry, hard mucus, and that there was cough, incontinence, and diarrhoea, and that the patient had to be fed with a nasal tube. He was very cyanotic, but breathed easily. The legs on the morning before death were icy cold. The pulse remained good until 6 P.M. when it became very feeble. The patient died an hour later, three days after admission.

Autopsy Findings

Body of man apparently about 30 years of age. Well developed, poorly nourished. No rash visible. Many sudamina.

Heart: Not dilated, muscle firm and normal in appearance. There is slight fibrous thickening of mitral valve which admits two fingers. The other valves are normal in appearance. The coronary openings are normal. There are a few small yellowish spots on the inner surface of the aorta.

Lungs: Normal in appearance. *No congestion.*

Abdomen: The intestines appeared normal externally.

Liver: On section the markings are indistinct. The color is rather pale brown.

Spleen: Adherent to surrounding structures and covered with fibrous adhesions. It is slightly enlarged and rather soft.

Kidneys: Normal in size; capsule strips easily. On section markings indistinct. Cortex shows yellowish mottling.

Specimens: Whole heart and pieces of organs.

AUTOPSY NUMBER 22. Patient of Dr. Smith.

Diagnosis: Typhus fever.

Died during the stage of defervescence or later.

Apparent Cause of Death: Late circulatory weakness.

Clinical Notes

The eruption was fading at the time of admission. The nurse says that at this time the patient was rather cyanotic and the pulse scarcely palpable, and that it improved later, but was never good. The patient gained a little at first and took food well until the last day. The stools were loose and there was slight diarrhoea. There was quiet, muttering delirium. The patient did not look as if dangerously sick. On the last day of life three saline enemata were given and all were retained. The patient got very cold six hours before death and died at 11 P.M.

Autopsy Findings

Body of man apparently about 35 years of age. Well developed and nourished. Much post-mortem discoloration.

Heart: Relaxed; muscle very flabby. Several small milk patches on epicardium. Edges of mitral valve show slight fibrous thickening. The orifice easily admits two fingers. The other valves appear normal.

Lungs: Pleural cavities normal in appearance. Anterior surface of lungs natural. Marked acute congestion posteriorly and especially at bases. No consolidation or atelectasis.

Abdomen: The intestines and stomach are distended with gas.

Liver: Normal in size and consistence, moderately congested.

Spleen: Few fibrous adhesions. The organ is several times the normal size and very soft.

Kidneys: Markedly congested; otherwise natural in appearance.

Specimens: Whole heart, and pieces of organs.

AUTOPSY NUMBER 23. (S. No. 95.)

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Coma, with cerebrospinal inflammatory phenomena and excess of cerebrospinal fluid.

Clinical Notes

June 12. Turkish prisoner, age 40. Admitted last night. Does not know how many days ill. Condition good.

Physical Examination: The patient looks comfortable, breathes through the mouth, respiration rapid and shallow, nostrils move with respiration. He is semicomatose, but replies to questions when roused. There is occasional dry cough.

The pupils are equal and very small. The conjunctivae are deeply injected. The tongue is brown, fissured, and dry. The pharynx and soft palate are red and glazed, with sticky mucus adherent.

The forehead and cheeks are flushed. There is a slight flush on the neck and on the upper sternum. The ears are not flushed.

The Eruption is seen on the lower part of the neck. It is profuse over the front and sides of the chest, on the upper abdomen and on the back, less abundant on the lower abdomen and upper arms, scanty on the forearms, legs, and hands, and slightly more marked on the feet. It consists of irregular, ill-defined macules, some large and some small. The color is purple with a pinkish tinge.

Heart: Size apparently normal, action rapid, regular. The aortic second-sound is of fair quality, the pulmonic second-sound is rather faint, and the first-sound at the apex has a valvular quality. The pulse is full and of the bounding type. The tension is low. The blood-pressure is 90/S.–50/D.

Lungs: There is no dulness or bronchial breathing. Many coarse, dry râles are heard and at the base of the right axilla some fine moist râles.

The Abdomen is soft, and there is slight general sensitiveness with voluntary spasm. The liver and spleen are not palpable but the splenic dulness is much increased.

The muscles of the neck are not sensitive but the neck can be bent forward only a little. Rotation is free. The muscles of the thighs and calves are sensitive to firm pressure. Those of the arms are not so. The knee-jerk is sluggish on the right and is not obtained on the left. Kernig's sign is well marked. Haemoglobin (Tallquist), 100 per cent.

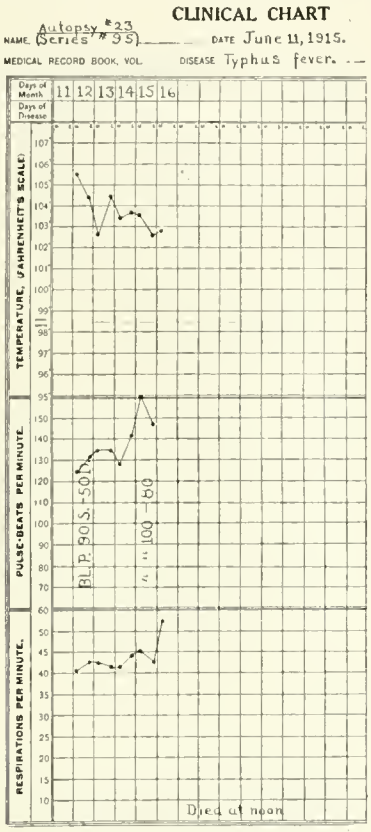
June 15. The patient's color is becoming dusky. He never sleeps. Digitalis has been administered subcutaneously because the patient takes medicine badly. He took food well the first day, but since then has taken little food or water.

He coughs a little but raises nothing. There are a few fine râles at the right base and many coarse and medium râles in the same region and extending upward to the mid-scapula.

Heart Sounds are of fair quality. The blood-pressure at 11.30 A.M. was 100/S.–80/D.

The eruption is fading. Some of the spots are brown and others are purple.

June 16. In the evening the patient became restless and made peculiar movements with the arms. There was *tonic spasm of the muscles of the arms,*



AUTOPSY NUMBER 23. Typhus fever. Coma and cerebrospinal inflammatory phenomena

and the fingers were clenched but not in the position of tetany. The knee-jerks were absent.

June 17. The patient's color has become almost leaden but the *pulse continues relatively good.* The respiration is more rapid.

The spasms of the arms have ceased, but stiffness of the neck has increased. Neither forward bending of the head nor rotation are now possible without pain. The patient is becoming comatose. The lungs show a few râles.

The patient died at noon.

Autopsy Findings

The muscles are not dry. Much blood escaped from the great vessels when the heart was removed. The subcutaneous fat is moderate in amount and very tough and dry.

Heart: Firmly contracted; muscle firm and normal in appearance.

Lungs: On the surface of the left lung at the apex are a few fresh adhesions and several small patches of blood-stained fibrin are adherent to the lateral and posterial aspects of the lower and middle portion. The lung tissue is leathery and pinkish on section. There is a small amount of oedema not confined to the bases. The bronchial mucosa is moderately reddened but not swollen. There is a little viscid exudation in the larger tubes. The condition of the right lung is practically the same as that of the left.

Abdomen: The intestines are not distended and are normal in appearance externally.

Liver: Yellowish, with nutmeg markings.

Spleen: Slightly enlarged, rather soft.

Kidneys: Appear normal.

Brain: On opening the skull a large quantity of fluid escaped. There was some blood with it which may have come from the veins or sinuses as a result of removing the skull.

The pia is markedly oedematous in the region of the motor area. The oedema is haemorrhagic and particularly so along the course of the arteries. There seemed to have been small haemorrhages in this region. These changes were more marked on the left side than on the right.

Specimens: Whole heart, and pieces of organs.

AUTOPSY NUMBER 24. (S. No. 94.)

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Exhaustion and circulatory insufficiency of vascular origin.

Clinical Notes

June 12. The patient arrived yesterday at 10 P.M. having travelled some distance on the train. He was too sick to be communicated with satisfactorily. At the time of admission the limbs were cold, the pulse of poor quality, and the heart sounds faint. Brandy was administered by mouth, coffee by rectum, and heaters were applied.

The face is flushed and the conjunctivae are injected. The pupils are of pin-point size. The tongue is dry with a brownish coat. The soft palate is red and dry. The patient breathes through the mouth rapidly and superficially.

The Eruption is profuse on the chest and abdomen. Less so on the arms, back, and legs. It is macular in form and purple in color.

The Heart Action is regular. The aortic second-sound is slightly accentuated and louder than the pulmonic second-sound. The first-sound is sharp and louder than the second at the apex. Blood-pressure, 105/S.–80/D.

The Lungs are clear except for a few râles at the right base.

The Abdomen is soft. The bladder is overdistended. (Catheterization was required daily.)

June 15. At noon the patient became almost pulseless. Almost immediately after a subcutaneous injection of ether the pulse returned. A few minutes later the patient swallowed a little brandy. Immediately after that the blood-pressure was 100/S.–90/D. Normal salt solution, 600 c.c., was then given intravenously. During the injection the heart sounds became louder and the aortic second-sound became accentuated. Immediately after the injection the first-sound was short but of fair quality, and the others were good. The second-sounds were about equal, the pulse was full, and the blood-pressure was 110/S.–90/D. At 4.45 P.M., about fifteen minutes after the infusion, the patient had a slight rigor which seemed to affect his condition little. When a nurse returned a few minutes later, the patient was again almost pulseless. After that he became very delirious and tried to get out of bed. In a short time he became quiet again and the pulse and heart sounds were once more of good quality.

The patient has been having diarrhoea and has taken little food for two days. He is rapidly losing flesh and strength.

June 16. During the night the patient again became pulseless and 360 c.c. of salt solution were given intravenously but the circulation improved little. The injection therefore was discontinued. The patient then received ether subcutaneously and the pulse improved.

This morning he became pulseless again. The respiration was very rapid. The patient was conscious but very weak.

Bronchial breathing of moderate intensity and a few râles were heard at the right base. The lungs were otherwise negative.

The pulse remained impalpable or nearly so throughout the day. In the morning, in spite of the *bad quality of the pulse*, the *heart sounds* were *loud* and *clear*. The patient died at 5 P.M.

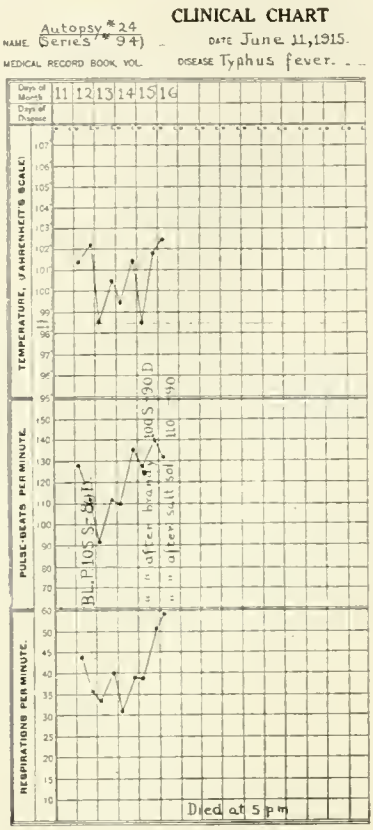
Autopsy Findings

The postmortem was performed sixteen hours after death.

Body of man apparently about 45 years of age, much emaciated, muscles not dry. Much blood escaped from the great vessels when the heart was removed. Subcutaneous fat moderate in amount. Very tough and dry.

Heart: Firmly contracted, muscle firm and normal in appearance, valves natural, coronary openings normal.

Lungs: The right lung in front and the left lung at the lower part posterially are bound to the chest wall by adhesions which appear neither recent nor very old. The left lung shows a moderate degree of passive con-



Autopsy Number 24. Typhus fever. Exhaustion and circulatory insufficiency

gestion especially at the base. The right lung shows a large area of *haemorrhagic oedema* in the *central portion* with increased consistency but no consolidation. The lower portion behind is atelectatic.

Abdomen: The cavity appears normal.

Liver: On section shows yellowish mottling.

Spleen: Slightly enlarged, rather soft.

Kidneys: Appear natural.

Specimens: Whole heart and pieces of organs.

AUTOPSY NUMBER 25. (S. No. 90.)

Diagnosis: Typhus fever.

Died during the postfebrile stage.

Apparent Cause of Death: Gradual exhaustion; inhalation pneumonia.

Clinical Notes

The patient was admitted to another ward on June 3. He had no eruption then. It was first noticed on June 7.

June 9. The patient refused to take medicine.

Digitalis, 0.00065 gm., was administered every four hours subcutaneously.

June 11. The patient breathes rapidly but easily and has occasional dry cough. He is mentally apathetic and his replies to questions seem incoherent. The face is not definitely flushed but the ears are red. The conjunctivae are not injected. The pupils are equal and of medium size. The lids of the right eye remain practically closed but there is no apparent muscular paralysis. The tongue shows a heavy brownish coat. The skin of the body is moderately pigmented, especially on the front of the chest.

Eruption: On the shoulders, the arms, the backs of the hands and feet, and the sides of chest there are many purple macules irregular in shape, varying in size. The abdomen is profusely covered with maculopapules. On the back and thighs there are a number of reddish-purple macules. The lower legs are free from spots but they present numerous recent scars and crusted ulcers, apparently syphilitic.

The Heart Action is regular, the sounds faint, the cardiac dulness diminished, and the pulse of low tension. Blood-pressure, 95/S.–75/D.

The Lungs are hyperresonant at the right base. There are many râles and the breath sounds are diminished. There are a few râles at the left base but no bronchial breathing.

The Abdomen is flat and shows slight general sensitiveness but no spasm.

The Spleen is not palpable but the splenic dulness is increased.

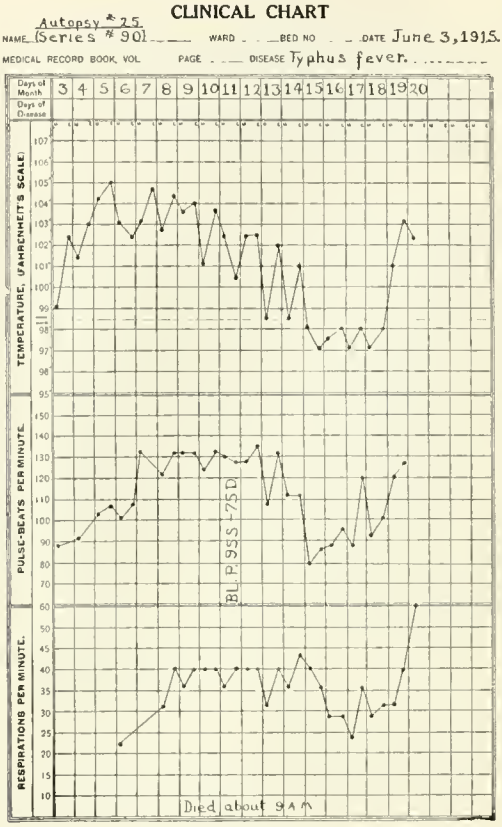
The knee-jerks are sluggish. The neck is slightly stiff and sensitive behind. The left leg can be raised perpendicularly without pain, but an attempt so to raise the right leg causes slight pain. The calves are not sensitive, but the thigh muscles are so. Haemoglobin, 90 per cent.

June 12. The patient began to be delirious at night on June 7 and has been so ever since. He has been very difficult to feed and has taken little nourishment. His condition is becoming serious. He was fed with a nasal tube last night. His mouth is very dirty and he refuses to have it cleaned. Evacuations are involuntary.

June 15. There is slight improvement today. The rash is fading and has become purple and brown; it is still clearly visible. Nasal feeding has been

continued with considerable difficulty. The patient is now beginning to drink a little liquid when given with bread. There is considerable muttering delirium this afternoon.

At night the patient is very delirious. He has taken so little liquid that 360 c.c. of salt solution were given intravenously at midnight. One hour



Autopsy Number 25. Typhus fever. Inhalation pneumonia

and a half after the infusion he had a severe chill. The salt solution had been freshly prepared with care.

June 17. The delirium is quieter today, and the patient weaker. A small abscess on the buttock was opened yesterday, and today another appeared on the thigh.

In the afternoon the patient was very weak and the pulse was of poor quality. Salt solution, 450 c.c., was given intravenously. Fifteen minutes later the delirium increased and the patient had a chill. A small dose of

morphine was given subcutaneously after which the pulse improved much and the patient slept well. The pulse remained good in the evening. The salt solution was used because the patient was taking practically nothing by mouth and fought off attempts to feed him with the nasal tube.

June 18. This morning the patient's condition is about the same. He is delirious, apathetic, and weak, but the pulse is of fair quality. He takes nourishment better.

Corneal ulceration began several days ago.

June 19. The patient is semicomatose and the pulse extremely bad.

June 20. For the last two days the patient's condition has been getting worse. Symptoms suggested pulmonary lesions, but no definite signs have been found. The lungs were not examined yesterday.

The abscess of the buttock became a slough and is increasing.

The stiffness of the neck continues slight this morning and the patient is practically pulseless and comatose. He died about 9 A.M.

Autopsy Findings

Postmortem performed one hour after death. Body much emaciated.

Heart: There is a milk-patch on the anterior surface of the heart. The left ventricle is firmly contracted. The right ventricle is flabby and perhaps a little dilated. The heart muscle is apparently in good condition. The aortic, mitral, and tricuspid valves show slight fibrous thickening. There are a few minute yellowish spots on the aorta.

Lungs: The left pleural cavity contains about 30 c.c. of pus. The pleural surface of the lung is cloudy and shows several small patches of fibrin. The right pleural cavity contains no pus but the surface of the lung is like that of the left except that the changes are less marked. In both lungs are numerous small, hard nodules, some of which, on section, yield pus. At the left base there is atelectasis. In the right lung a bright red, narrow area of consolidation follows the posterior margin.

Abdomen: The intestines appear normal externally.

Liver: Shows slight nutmeg markings.

Spleen: Firm, and slightly enlarged.

Kidneys: Capsules adherent in places, cortex variable in width, markings indistinct, color rather pale.

Specimens: Pieces of organs.

TYPHUS FEVER, FATAL CASES
NO AUTOPSY

Series Number 87. Patient of Dr. Holmes.

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Severe toxaemia with general symptoms.

Clinical Notes

A Russian physician, admitted May 21. A slight eruption was first observed on that day.

May 27. Physical Examination: The apparent age is about 23. The patient lies on the back propped up. He is conscious but the mind is clouded. The eyes are closed, the respiration is rapid and shallow. The cheeks and eyelids are brightly flushed and the ears are bright red. The arms twitch occasionally, the hands move aimlessly and pick at the bedclothes.

The eruption is profuse on the chest, and dull red in color. The color partly disappears on pressure. The spots are irregular in size and shape. Most of them are macular but on very close inspection a few are seen to be slightly elevated. The elevation is more easily appreciated by palpation. The rash is clearly seen on the backs of the hands, and is abundant on the arms, abdomen, and legs. On the abdomen are a few maculopapules which are darker red and more elevated than the others. From these the color does not disappear on pressure. The rash as a whole is beginning to assume a purple tinge.

The *Heart Action* is rapid and regular. The first-sound is faint and the second-sounds are accentuated. The pulse is large and of the bounding type.

Lungs: No râles are heard in front. The backs were not examined. There is an occasional cough like that of bronchitis.

June 1. The patient's condition has been critical for several days. The respiration is very rapid and the pulse is very rapid and of poor quality. There is slight cyanosis. When the patient coughs there is rattling in the throat but he is unable to raise anything.

Three days ago he grabbed his chart and carefully examined it. Yesterday he was too sick to do this. He lies most of the time with eyes closed and when approached looks nervously from side to side.

The chin twitches most of the time and the other muscles of the face move continually. The hands move convulsively and in a futile manner.

The eruption is purple and is beginning to fade. The bases of the lungs are free from râles. There is no dulness or bronchial breathing. Nourishment is taken fairly well. There is considerable perspiration.

Abdominal distention is now very marked. The colon can be felt through the abdominal wall. The distention can be reduced temporarily by enemata and the pulse rate then falls but the distention returns in a short time and then the pulse rate rises again. The temperature remains high.

June 2. The patient died last night.

Series Number 21. Patient of Dr. Holmes.

Diagnosis: Typhus fever.

Died during the stage of nervous depression.

Apparent Cause of Death: Pulmonary oedema, sudden asphyxia.

Clinical Notes

May 1. Present Illness: A Serbian officer, said to have been ill six days before admission. He complains of pain around the eyes and in the back of the head, but not in the legs. There is cough and a little expectoration.

Physical Examination: The apparent age is about 35. The patient is well developed and nourished. The face is much tanned, the ears are red, and the hands are slightly so. The tongue shows a white coat. The conjunctivae are not injected. The pupils are equal and of normal size.

The Eruption is profuse and consists of pink macules on chest, abdomen, and arms. The hands, face and neck are free from spots.

The Heart Action is rapid and regular. The sounds are of good quality and there are no murmurs. A few coarse râles are heard at the apices behind.

The Abdomen is negative. The spleen is not palpable and splenic dulness is not increased.

The Neck is slightly stiff. There is a slight Kernig's sign associated with muscular spasm but no pain. The calves are not tender.

May 3. The diazo-reaction is mildly positive.

May 5. The severity of the illness is increasing. The patient is mentally dull and confused but recognizes people.

There was epistaxis today, moderate in amount.

The expectoration is considerable in quantity and very tenacious. The breathing is rapid and shallow. Many râles, most of which are of the coarse, dry variety, are scattered throughout the lungs.

The rash is fading and turning brown.

Blood-pressure, 90/S.–55/D. Haemoglobin, 85 per cent.

May 7. There is an occasional spasm of hiccough. The patient is cyanotic. The breathing is rapid and makes a whistling sound at the nose. The nostrils move with respiration and there is a rattle in the throat. The cheeks are flushed. The forehead, which was very white on admission, is now slightly pigmented.

The heart sounds are obscured by coarse râles. Blood-pressure, 110/S.–55/D. The patient takes food badly but water and lemonade freely.

May 9. This afternoon, in the absence of the physician in charge of the ward, the patient was reported to me as being in a dangerous condition. When seen within a few minutes he was found gasping and unconscious but with a full, strong pulse which was not rapid. There was a loud rattle in the throat. The patient was quickly turned on his side and the jaws held open. He then began to draw deep breaths at long intervals but in two or three minutes the pulse and respiration both stopped and the patient died.

PROBLEMS IN DIAGNOSIS

The three following cases, Autopsies Nos. 2, 11, and 26, illustrate either errors of diagnosis or interesting complications of typhus fever.

Autopsy Number 2.
Patient of Dr. ——.
Clinical Diagnosis: Typhus fever.
Pathological Diagnosis: Malignant endocarditis.

Autopsy Number 11.
Patient of Dr. ——.
Clinical Diagnosis: Typhus fever.
Pathological Diagnosis: Typhoid fever with perforation of the intestine.

Autopsy Number 26.
Patient of Dr. Smith.
Clinical Diagnosis: Typhus fever (?).
Pathological Diagnosis: Endocarditis, typhus fever (?).

Clinical Notes

The patient was admitted June 14. His age was 30 and he is said to have been ill four days. No eruption was seen on admission or later. The patient was conscious at first and became comatose later. The breathing was noisy and difficult. There was muscular twitching. The general appearance of this patient suggested typhus fever. On June 22 the neck was markedly stiff and there was a slight Kernig's sign. The patient died at 3.40 P.M.

Autopsy Findings

Postmortem performed five hours after death. Body fairly well nourished.

Heart: There is a large milk-patch on the anterior surface. The left ventricle is firmly contracted, and there is no dilatation of any of the chambers. The mitral valve shows a continuous row of small, pearly white, soft vegetations along the edge. Beneath the endocardium a little above one of the cusps is a small area of haemorrhage. There is no ulceration. The other valves are natural. The intima of the aorta shows a few very small yellowish patches. The coronary openings are free.

Lungs: The left shows much oedema, especially at the base. The base of the right is oedematous and atelectatic.

Abdomen: The intestines are normal in appearance. The lower part of the ileum was opened and no ulceration or swelling was found but the *mucous membrane showed many minute red dots.*

Liver: Much congested.

Spleen: Normal in size, rather firm.

Kidneys: Extremely congested.

Brain: Shows whitish streaks along some of the larger arteries on the upper and lateral surfaces of the hemispheres. No pus on the meninges. Cranial fluid perhaps a little in excess. Meninges not oedematous. Base of brain natural. Lateral ventricles contain a pale and slightly turbid fluid. Lumbar puncture after death showed that the fluid was not under tension. Several cubic centimeters were removed with a syringe. The fluid was clear and greenish yellow in color.

Series Number 33.

Diagnosis: Scabies, typhus fever (?).

Clinical Notes

May 8. Serbian, apparent age about 20. The patient says he has had typhus for a month which probably means that he has had scabies for a month.

Physical Examination: The patient is well developed and nourished. The skin and mucous membranes are pale. The conjunctivae are slightly injected.

The skin of the body and face is somewhat pigmented and shows many brown macules of various sizes. There are many excoriated papules upon the front of the chest, abdomen, upper arms, axillae, groins, wrists, and genitals. There are no such papules below the knees. The forearms, wrists, and hands show many crusted papules of moderate size and there are similar ones on the lower legs.

On the chest there are a *few pink macules* which might be interpreted as a scanty eruption in a mild case of typhus.

The other lesions, clearly, are due to scabies.

Heart and *Lungs:* Negative.

Abdomen: Soft, not tender. Spleen not palpable; splenic dulness not increased.

Knee-jerks present. No stiffness of neck or legs.

Haemoglobin (Tallquist), 100 per cent +. Blood-pressure, 105/S.–65/D.

May 13. Throat slightly red. Heart, lungs, and abdomen negative.

May 14. Skin improving under treatment for scabies. Few brown spots remain.

June 1. Patient discharged well.

NOTE: The temperature curve in this case points to an acute infection of some sort and the small amount of local infection of the skin lesions can-

SERIES NUMBER 33. Scabies, (?) typhus fever

not explain it. Although more irregular than the curve usually is in typhus the chart suggests this disease and the pink macules above mentioned strengthen such an hypothesis.

SERIES NUMBER 33A.

Diagnosis: Gangrene of foot and leg, probably a sequel of typhus fever.

Clinical Notes

April 26. A Serbian. Brought in with a number of typhus patients that arrived together on a train. Said that he had been ill eight days.

Spots were seen which may have been a fading typhus rash, but which were not sufficiently definite for a positive diagnosis.

At the time of admission there was pronounced discoloration of the left foot and of the leg halfway to the knee, a line of demarcation existed at the "point of election."

May 5. The patient was transferred to a surgical hospital for amputation of the leg.

NOTE: This case illustrates the difficulty of satisfactory diagnosis after the eruption has faded.

SERIES NUMBER 88.

Diagnosis: Pappataci fever (?). Abortive typhus (??).

Clinical Notes

May 26. The patient has been sick two days. He complains of pain in the temples, thighs, and back.

Physical Examination: The patient is rather drowsy, but mentally clear and alert when aroused. The pupils are equal and of moderate size. The conjunctivae are moderately injected. The tongue shows a thin, white coat. The throat, the soft palate, the pillars of the fauces, and the pharynx are red. There are no spots on the mucous membranes.

The Heart is negative, the pulse of good quality, and the blood-pressure, 90/S.–60/D. Haemoglobin, 80 per cent.

The Lungs and *Abdomen* are negative. The splenic dulness is not increased and the spleen is not palpable.

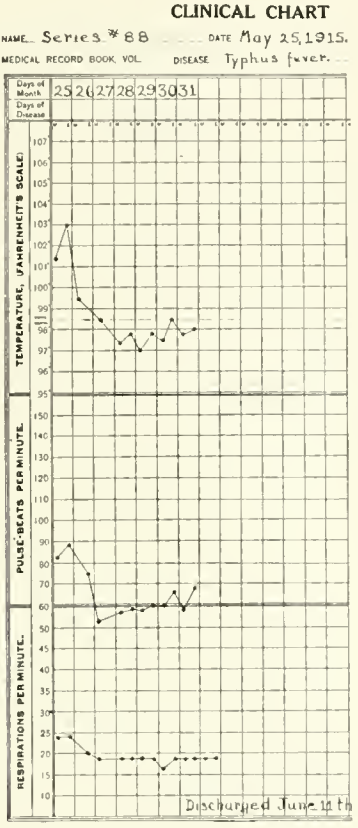
The knee-jerks are present. There is no stiffness of the neck or legs. The thigh muscles are slightly sensitive to firm pressure.

Skin: The face is covered with a red flush which extends two-thirds of the way down the neck and, in front, covers a V-shaped area extending on to the sternum. A slighter flush extends over the lower part of the neck to the shoulders and over the clavicles to the second ribs where it gives place to rose-colored macules. The ears are very red. On the sides of the chest, the flanks, and the abdomen there are a few bright red, clearly defined spots the size of a pinhead and a few purplish spots of about the same size which do not disappear on pressure. (Old flea bites?)

On the inner aspects of the arms and of the flanks "taches bleuâtres" are numerous. In the center of some of these is a bright red, circumscribed spot like those already described on the sides of the chest and flanks. These spots are believed to have been caused by bites.

On the hips and on the backs of the hands are a considerable number of maculopapules some of which are capped by a small vesicle. The nature of these spots is uncertain. They resemble acne more than anything else.

June 2. On the day after admission of the patient the temperature dropped to normal. On the same day a rash consisting of groups of very



SERIES NUMBER 88. Pappataci fever (?). Abortive typhus (??)

small, irregular papules was found on the flanks and sides in the morning. In the afternoon it had nearly disappeared and in the evening there was no sign of it. The patient's condition today is excellent.

June 11. With the exception of a rise of temperature to 99° on one day, there has been no recurrence of fever. The patient is to be discharged tomorrow.

NOTE: The probability in this case seems in favor of the diagnosis of pappataci fever.

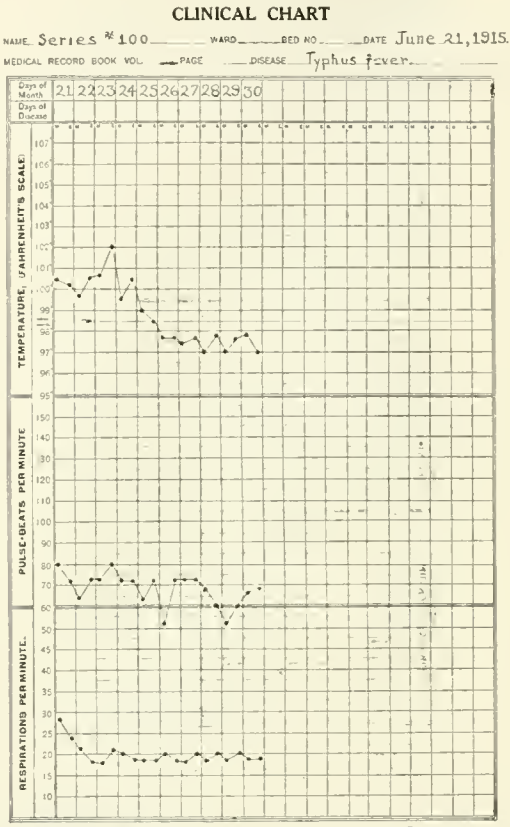
SERIES NUMBER 100.

Diagnosis: Pneumococcus bronchitis. Typhus fever (??).

Clinical Notes

June 21. Admitted to hospital today. Duration of illness ten days.

Physical Examination: The face is flushed and the conjunctivae are injected. There is pink mottling of the skin on the chest and abdomen but



SERIES NUMBER 100. Pneumococcus bronchitis. Typhus fever (??)

there are no macules or papules. The tongue shows a brown coat. The mind is clear and the general condition is good. The spleen is not palpable.

June 24. There is profuse purulent expectoration. The face is still a little flushed and a band of injection extends across the conjunctivae.

The lungs were negative yesterday and today.

The patient is improving and does not look seriously sick. Microscopical examination of the sputum shows pneumococci in great numbers and few other bacteria. No tubercle bacilli were found.

NOTE: The most probable diagnosis seems to be bronchitis caused by the pneumococcus. The "mottling" on the chest may have been due to the application of a counterirritant of some sort.

There seems no reason for believing the case to be one of typhus fever although the patient was sent in as such.

PART III

LABORATORY EXAMINATIONS IN TYPHUS FEVER

By ANDREW WATSON SELLARDS

Introduction

In order to complete the arrangements of the commission for conducting sanitary work, a central laboratory was organized by Dr. Hans Zinsser in Skoplje at the Lady Paget Hospital. The scope of this laboratory included the preparation of various vaccines, the sanitary examination of water supplies, and more particularly, special investigations of typhus fever. The opportunity was afforded me to carry out clinical laboratory examinations on typhus fever patients.

The general findings in typhus fever were observed with the special object of differentiating this disease from other infections which were prevalent and in which an early clinical diagnosis could not be made. Of the acute infections which gave rise to confusion, the two most troublesome ones were typhoid and relapsing fever. Indeed the clinical similarity in the onset of these three diseases gave rise to a local custom in the Balkan States of designating them all by the one name "typhus." It was often only by the context that one could determine whether reference was made to *typhus exanthematicus, typhus recurrens,* or *typhus abdominalis.* The rapid clinical differentiation of typhus and relapsing fever would have been advantageous since, in the management of the sanitary work, it had seemed desirable to the authorities to reserve the Lady Paget Hospital solely for typhus cases. Once the cases had been admitted, the prompt diagnosis was important to prevent, as far as possible, the development of cross infections in the hospitals.

Examination of the Blood in Typhus Fever

In the literature on the clinical microscopy of the blood in typhus fever certain important statements occur which, for the most part, have remained unconfirmed. Even as regards the actual blood counts, and the morphology of the blood-cells, the statements are somewhat conflicting. In searching for parasites, Ricketts and Wilder [1] in a preliminary note reported the finding of bacteria in blood films stained by Giemsa's method; with similar preparations Prowazek [2] noted the occurrence in the white cells of inclusion bodies of the general character of the chlamydozoa.

Red Blood-Cells

Prompt confirmation was obtained of the high count of red blood-cells, figures of 5,500,000 and 6,000,000 being common, the haemoglobin content being increased often in greater proportion than could be accounted for by the increase in the number of red cells. The percentage of haemoglobin was determined with a Sahli apparatus standardizing the instrument by comparing it with several normal healthy adults and considering this value as 100 per cent. The blood examined was taken in all cases from the ear. This increase in cell count and haemoglobin was most marked at the height of the infection. With the progress of the disease, the count usually fell to normal or even to slightly subnormal values; a definite anaemia did not develop in typical cases. Some of the conditions bearing on this increased count were considered. Clinically, there was no increase in the size of the spleen in contrast to the splenomegaly which sometimes accompanies polycythaemia. Many of these patients showed the effects of depletion in their supply of fluids. The explanation of this lay not in an excessive loss of fluid due to any effect of the typhus infection, but to the inability of the patients to obtain water during their long journey to the hospital. In order to determine in how far the poly-

[1] Ricketts and Wilder: Jour. Am. Med. Assn., 1910, liv, 1373.

[2] Prowazek: Med. Rec., N. Y., 1915, lxxxviii, 21; Beitr. z. Klinik d. Infections. u. z. Immunitätsforsch., iv, No. 1.

cythaemia was due to deprivation of water, a series of counts was made upon selected cases in whom the therapeutic injection of salt solution was required. These injections were made intravenously, in quantities of one-half to three-fourths of a liter. The first injection often showed surprisingly little effect upon the blood-count; repeated injections usually reduced the red count and the haemoglobin considerably. The values often remained slightly higher than normal even after sufficient fluid had been injected to restore the tissues approximately to their normal condition. Signs of this restoration consisted chiefly in the return of the elasticity of the skin, the improvement of the pulse, and the free secretion of urine. It seemed justifiable to conclude that the deprivation of water was responsible in a large measure for the high red counts and high haemoglobin, though one could not exclude the possibility that other factors may play a minor rôle.

In fresh preparations and in stained smears the red cells were essentially [1] normal. In a small proportion of the cases the red cells showed coarse basophilic stippling and occasionally polychromatophilia. This feature occurred indifferently both in the cases with moderately low counts and also in some instances in which the red cell count was as high as 6,000,000.

White Blood-Cells

In regard to the white blood-cells there is a prevalent opinion that a leucocytosis of high grade often occurs late in the disease, characteristic large mononuclear cells appearing in the blood. The total number of white cells was found to be rather variable. Often the count was normal or a little high. In a few instances a marked leucopoenia was present. These leucopoenias, however, were rather transient instead of persisting over a period of days or weeks as in typhoid fever. Occasionally a striking leucocytosis developed during the second week of the disease. Thorough examination often revealed some focus of

[1] The Giemsa stain was used exclusively, partly because this stain keeps very well in warm climates and also because the work of Ricketts and Prowazek is based upon smears stained with Giemsa's method.

secondary infection. Two patients with high counts in whom no complications could be found developed, after a few days, a small patch of pneumonia. A few cases developed leucocytosis, however, in which no suggestion of secondary infection could be detected.

The differential counts showed considerable variation. Frequently the mononuclear cells were increased at the expense of the polymorphonuclears and often the large non-granular mononuclear cells were unusually prominent. These cells were often difficult to classify. Polymorphonuclear cells that appeared to be rather young were seen not infrequently. An occasional neutrophilic myelocyte was seen in the peripheral blood. These were rare being by no means as frequent as in some of the high grade bacterial leucocytoses.

A thorough examination of the blood in ten active cases of the disease failed to reveal either the bacilli described by Ricketts or the inclusion bodies of Prowazek. Most of these patients were examined for the first time at about the fourth or fifth day of the disease and subsequently throughout the remainder of the course at intervals of two or three days.

The platelets were abundant in the blood smears and they were normal in appearance. The bleeding time and the coagulation time were within normal limits. The latter was determined by drawing the blood in a syringe from a vein and noting the time required for coagulation in a test tube.

It is not infrequently stated that the blood of typhus cases is very prone to give the reactions of agglutination and complement fixation with various antigens. Cameron [1] has emphasized the occurrence of positive Widal reactions with the sera of typhus patients. In view of his observations, some macroscopic agglutination tests were carried out in the Lady Paget Hospital using *B. typhosus* and the two paratyphoid strains, A and B. Twenty typhus cases were examined three of which were active and the others were convalescent. No positive reactions were obtained with either of the two strains of paratyphoid. With the typhoid strain there were five cases which

[1] Cameron: Brit. Med. Jour., 1915, i, 785.

TABLE I. — BLOOD COUNTS AND HAEMOGLOBIN DETERMINATIONS ON TYPHUS CASES UPON ADMISSION

Case no	Day of disease	Red cell counts Millions per c.mm.	White blood-cells Number per c.mm.	Haemoglobin Sahli
1	4	4,0	12,000	120
3	8	6,0	6,000	135
8	10?	5,6	5,000	95
9	8	5,5	4,600	125
10	8	5,9	16,600	130
11	5	4,0	6,000	90
15	14 *	4,0	7,200	100
16	18 *	4,1	3,200	110
17	14 *	5,6	6,000	120
18	5	4,7	1,500	95
19	5	4,4	8,800	105
20	16 *	3,9	4,800	85
21	6	3,5	3,900	110
35	5	4,5	7,600	110
41	6	4,7	3,700	110
45	8?	5,0	4,000	115
46	2	5,1	10,600	115
47	7	4,9	4,800	115
53	?	5,6	4,300	130
55	4	6,2	5,800	145
56	6	5,2	10,200	115
57	12	4,6	7,800	110
58	10	5,0	15,000	115

* These are patients who reported themselves ill from some unknown cause and in whom typhus fever developed as an intercurrent infection.

gave good agglutination at a dilution of 1:25, but not at 1:50. In the entire series there was but one case which gave agglutination at 1:50 and the clinical diagnosis of typhoid fever had already been made in this patient. In the cases agglutinating at 1:25 no record was available in regard to their previous history of typhoid fever and of antityphoid vaccination; consequently, even if an occasional positive Widal had been obtained in the typhus cases it would not have been of any especial significance.

For completeness sake some of the data of the blood counts are appended. The data in regard to the time of onset of the disease are extremely unsatisfactory. Many patients were too

ill to give a reliable history; others did not consider themselves ill unless a rash or high fever developed. The data for the "day of the disease" as given in Table I are compiled in part from the history of the patient and in some cases from the apparent stage of the disease as judged by the clinical findings.

In ten additional cases occurring toward the close of the epidemic and showing no complications, the white count during the first week of the disease varied from 3800 to 13,000.

In Table II some typical differential counts are recorded.

TABLE II. — DIFFERENTIAL COUNTS ON TYPHUS CASES

Case no.	Day of disease	Total count	Polymorphonuclear neutrophiles	Large and small lymphocytes	Large mononuclears	Transitional cells	Unclassified cells	Eosinophiles Number seen
1	4	12,000	92 %	3 %	4 %	0 %	1 %	None
3	8	6,000	77	13	10	0	0	One cell
8	10?	5,000	72	18	6	2	2	Two cells
9	8	4,600	82	8	6	0	4	None
10	8	16,600	72	17	8	2	1	One cell
11	5	6,000	72	20	6	1	1	None
17	?	6,000	72	20	4	2	2	
18	5	1,500	47	31	15	3	3	None
19	5	8,800	73	17	2	5	3	None
20	?	4,800	76	18	2	2	2	Two cells
21	6	3,900	70	18	6	3	3	None
87	4	12,000	76	21	2	1	0	None

These percentages are based upon counts of 300 cells.
The eosinophiles were unexpectedly scarce, never being as high as one per cent.

An attempt was made to follow the blood-counts from the onset of the disease throughout its course in a small group of uncomplicated cases. The effort to secure such a series was not very successful. In Table III, although the exact day of the onset is not accurately known, still the figures give a very fair idea of the stage of the disease. These counts were made from uncomplicated cases or at least the patients were free from complications at the time these observations were made. As regards the effect of complications there seemed to be a comparatively large proportion of cases in which pyogenic abscesses failed to produce a polymorphonuclear leucocytosis.

TABLE III.—WHITE BLOOD COUNTS AT VARIOUS STAGES OF THE DISEASE

Case No.	Day of Disease																						Ultimate Result
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	24	25	
1			12,000						16,000				10,700			7,200							Recovery
3						8,600	6,000						6,200				5,000			8,600			Recovery
9							4,600			18,400		6,800		6,400					4,500				Recovery
10							16,600			14,200		9,700		6,300					5,700				Recovery
18				1,500		2,700			3,900			5,500										9,400	Recovery
19				8,800		12,000			9,500												16,000		Recovery
20															4,800		9,000	9,500		6,000			Recovery
21					3,900		4,800			8,800					3,000								Death
23		5,000		5,600			6,300																Recovery
24			5,500		12,000			9,000															Recovery
56					10,200						3,500			9,000			13,800						Death
86									13,300			9,900			16,000								Recovery
88[1]	2,500	2,400		3,800																			Recovery

[1] Question of differential diagnosis between pappataci fever with rash and mild typhus.

Examination of the Urine

Examination of the urine showed an almost constant and early development of some inflammation of the kidney. Moderate amounts of albumin were present and granular casts were fairly numerous. These signs were usually transient, clearing up promptly with the drop in temperature. In one instance only, a severe nephritis developed during the height of the disease which did not entirely clear up during convalescence; in this case a preëxisting nephritis could not be excluded.

The diazo-reaction was found to be almost constantly present and usually very strong. However, it did not occur early in the disease and it was not of definite value in the differentiation of early or doubtful cases.

Differential Diagnosis

We do not at present possess routine methods which are adequate for the recognition of atypical cases of typhus fever or for the early diagnosis before the typical clinical picture has developed. Among the French physicians a high percentage of cases are frequently diagnosed as typhus "sin exanthem"; while this type may occur more or less frequently, it is a diagnosis which is extremely difficult to establish. The more common laboratory procedures give evidence in typhus which is essentially negative in character. Of the few positive findings, the occurrence of the diazo-reaction in the urine and the tendency of the mononuclear cells of the blood to increase were of only very minor assistance. The diagnosis of typhus by the laboratory findings must be made by exclusion. This is frequently unsatisfactory for its differentiation both from typhoid and from relapsing fever.

The application to typhus fever of some of the more elaborate experimental procedures gives results which are characteristic. The inoculation of the virus of typhus fever into monkeys and guinea pigs often gives rise to a characteristic temperature curve; studies of complement fixation and agglutination to *B. typhi exanthematici* have in the hands of Plotz,

Olitsky, and Baehr [1] given results of diagnostic value. The transmission of the virus to lower animals is at present out of consideration as a diagnostic method; the results are so inconstant that the procedure is suitable only for the laboratory study of typhus. Jahlous [2] reports that there is a general tendency of the serum of typhus cases to give non-specific complement fixation with the Wassermann antigens. This possibility in typhus fever should be taken into consideration in any diagnostic methods involving complement fixation. Olitsky [1] finds that an antigen of *B. typhi exanthematici* fixes complement readily with the sera of typhus cases but not with other sera. Furthermore, antigens prepared from other bacilli fail to fix complement with typhus sera. Olitsky's results though very striking have not yet received any wide confirmation. The final establishment of diagnostic aids by the use of complement fixation either with a specific or a non-specific antigen requires an enormous amount of empirical work carried out preferably in a number of different laboratories.

Bacteriological Cultures in Typhus Fever

In the search for the specific organism of typhus fever, the blood is the most suitable material for examination. Injection of blood from typhus patients into normal men reproduces the disease, thereby demonstrating that the virus occurs in the circulating blood. Numerous bacteriological cultures have proven that the virus as it occurs in the blood is practically pure.

Of the many organisms that have been described as the specific aetiologic factor in typhus fever there is none on which so much work has been done or for which so much favorable evidence has been offered as in the case of the anaërobic bacillus described by Plotz and his associates. The following attempts at the confirmation of this organism were made in Belgrade and its vicinity. The technique described by Plotz

[1] Plotz, Olitsky, and Baehr: Jour. Infect. Dis., 1915, xvii, 1.

[2] Jahlous: Jour. Med. Research, 1914, xxx, 131; Delta, Centralbl. f. Bakteriol., I, Abt., Orig. 1915, Bd. lxxvi, 50.

was followed carefully but in view of the proportionately large number of negative results obtained by Dr. Zinsser in Skoplje some additional cultures were made with certain minor modifications of the Plotz technique. These consisted in an enrichment of the medium and an increase in the degree of anaërobiosis. Three samples of ascitic fluid were used. They were free from bile and the specific gravity varied from 1.015 to 1.018, but in view of the possibility that they might not be entirely suitable for the growth of the Plotz bacillus pieces of kidney tissue were added in some instances. This procedure had given successful results in Plotz's experience but was regarded by him as an unnecessary refinement. Some of the Plotz cultures to which kidney tissue had been added were given a higher degree of anaërobiosis by placing the tubes in a jar from which the oxygen had been absorbed by yellow phosphorus.

In the selection of cases, only those patients were chosen from whom cultures could be made some time during the first half of the period of the exanthem, except in one instance when a fulminating case was cultured who died eight hours later. The cultures from this patient developed numerous colonies, some cocci growing aërobically, and some bacilli growing anaërobically; the latter were longer and coarser than the organism described by Plotz. Cultures from twelve additional cases remained sterile for one month with the exception of an occasional mould or coarse coccus growing on the surfaces of the media toward the end of this period. No anaërobic growth occurred either in the cultures made by Plotz's technique or in those tubes to which kidney tissue was added some of which were placed in an anaërobic jar. Five of these twelve cases were cultured either on the first or second day of the appearance of the rash. Moreover, the work was done under very favorable conditions. The laboratory at Belgrade was housed in a substantial building and was well equipped with modern French apparatus. In Serbian Macedonia it had been necessary to work practically under field conditions with a laboratory set up in what was formerly a Turkish artillery shed, where

the exposure to dust storms added greatly to the difficulty of the work.

It is hard to understand this failure to obtain the Plotz bacillus under favorable conditions in view of the practically constant recovery of the organism from acute cases by Plotz and his associates. Although it is exceedingly treacherous to work with unheated and unsterilized media, yet in a large series of control blood cultures Plotz failed to obtain this organism in a single instance. It is evidently a highly parasitic organism but I am not yet convinced that it occurs only in typhus fever or that it is pathogenic for man. Although Plotz has collected a large amount of evidence in favor of this organism, there are still some serious objections to its acceptance.

Anderson has pointed out that the cultures on injection into animals give rise to a transient fever which does not especially resemble the temperature curve of typhus fever; moreover these animals on subsequent injection with typhus fever virus may react with a typical rise in temperature. If a liberal dose of the living organism fails to protect an animal against typhus virus, some doubt is raised as to whether the usual small vaccinating dose would give efficient protection in man.

In addition to the failure to obtain the anaërobic bacillus isolated by Plotz, I was likewise unable to confirm the work of Topley.[1] In kidney tissue ascitic fluid agar, Topley reports the clouding of the media due to the growth of minute cocci or bacilli. On this medium, cultures of a diplococcal organism were obtained in each of eight cases.

As regards the bacteriological examination of the urine no confirmation could be obtained of the small coccobacillus reported by Hort and Ingram.[2]

Specific biologic reactions such as agglutination and complement fixation were not attempted in view of the negative results in these cultures and the inability to secure a strain of Plotz's organism at this time.

[1] Topley: Jour. Roy. Army Med. Corps, 1915, xxv, 215.
[2] Hort and Ingram: Brit. Med. Jour., 1914, ii, 15.

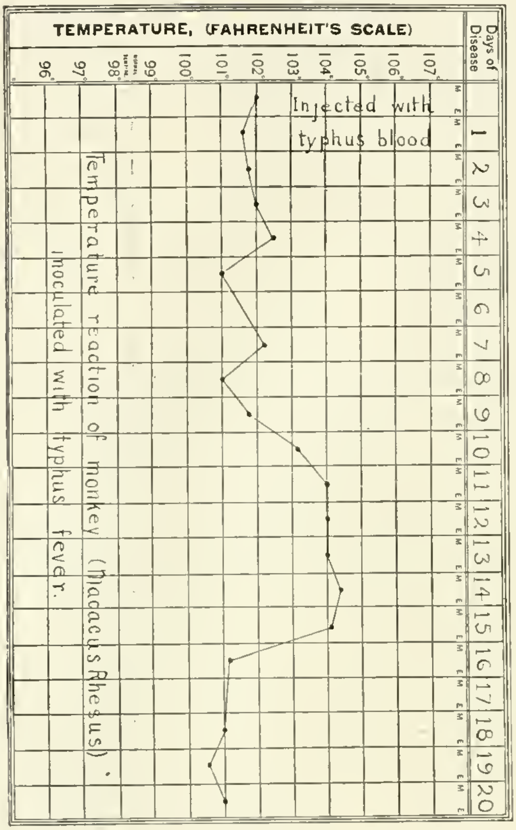
Animal Experimentation

The reported transmission of typhus to animals, especially to guinea pigs, has given rise to considerable confusion. The recognition of the disease depends almost wholly on the temperature reaction. The highest febrile reaction produced by the typhus virus is usually not greater than the maximal normal temperature of the guinea pig. However, after a definite incubation period, this maximal temperature is sustained steadily over a period of several days without remissions such as occur in normal animals. There may be considerable doubt about the specific nature of the rather transitory rises in temperature following the injection of the virus of measles and scarlet fever into lower animals. However, in the case of typhus fever it would seem that guinea pigs are definitely susceptible and permit the growth and multiplication of the virus for a time. However, not all individuals react. Indeed, there is every gradation between a typical febrile curve and no reaction. Since the normal temperature of the guinea pig varies considerably, it is often impossible to interpret mild reactions. Indeed, some of the important statements in the literature are based upon the interpretation as positive of reactions which in no way differ from normal fluctuations in temperature.

In the following work, the animals were inoculated from cases of typhus during the first or second day after the appearance of the rash. Guinea pigs were injected intraperitoneally with 3 to 5 c.c. of blood from several typical cases but the reactions which followed were not satisfactory. Moreover, after a period of incubation subinoculation from the first guinea pig to a second one was likewise unsuccessful. A reaction in guinea pigs corresponding to those described by French and American authors was obtained, however, by passing the virus first through a monkey and then through a guinea pig, analogous to the method for securing the infection of rats with relapsing fever. The reaction in a monkey produced by an injection of blood from a human case is illustrated in the accompanying chart, together with the chart of a control animal. Blood cul-

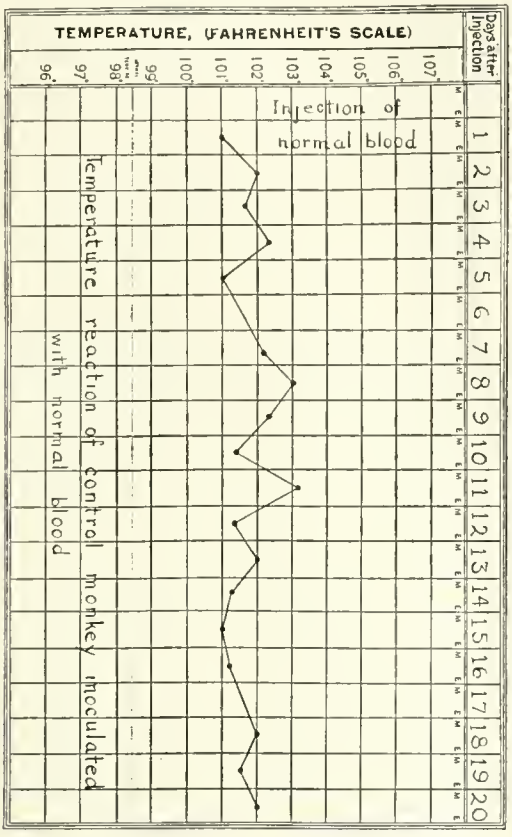
tures taken from this monkey on the second day of the fever were negative.

Such a slight rise of temperature over a short period of time is, in a single instance, without significance. The evidence,



however, that the virus of typhus multiplies in the monkey and guinea pigs and is responsible for this rise in temperature lies in the fact that one can in a certain proportion of cases duplicate these results; moreover the monkeys appear distinctly ill during the febrile period. In contrast to this febrile reaction, an instance was observed of natural immunity in the monkey, a feature that was emphasized by Anderson and Goldberger. The frequency of the occurrence of immune animals

and of indefinite reactions renders the procedure extremely tedious and treacherous as a laboratory method. It is considered that one of the most essential features for further progress in animal experimentation is the development of some



means for the recognition of typhus in animals. This is especially necessary in view of the great importance attached to the experiments on the louse transmission of typhus in the lower animals.

Question of the Mode of Transmission of Typhus Fever

Some of the cardinal features concerning the mode of transmission of typhus fever are still undetermined. In the case of malaria and yellow fever it is not only proven that these diseases are commonly transmitted in man by mosquitoes but it is clearly established that they are not propagated in any other manner. This, of course, is an extremely fortunate circumstance in the management of these two diseases. In typhus fever there is ground to believe that it may be transmitted either by droplet infection or by the louse. The evidence regarding louse transmission is in a somewhat confused condition.

The transmission of typhus to monkeys by the human body louse has been investigated by three groups of authors, namely, Nicolle and his associates,[1] Ricketts and Wilder,[2] and Anderson and Goldberger.[3] These authors have all arrived at the same conclusion: namely, that typhus is transmissible to the monkey by the body louse. However, it is very striking that the data and the fundamental premises of the various authors frequently vary widely and even conflict seriously. Thus the results on which one group of authors base their conclusions would frequently be unacceptable to the other two. Ricketts and Wilder considered that all normal monkeys are susceptible whereas Anderson and Goldberger frequently found natural immunity in monkeys. Nicolle found that monkeys which were bitten by lice without developing fever were subsequently susceptible to the injection of virulent blood, whereas Ricketts obtained the opposite result. Nicolle as well as Anderson and Goldberger determined infection in the monkey by the febrile reaction whereas Ricketts in his experiments on

[1] Nicolle, Comte, and Conseil: Ann. de l'Inst. Pasteur, 1910, xxiv, 261; Nicolle and Conseil: ibid., 1911, xxv, 109; Nicolle, Blanc, and Conseil: Compt. rend. Acad. d. sc., 1914, clix, 663.

[2] Ricketts and Wilder: Jour. Am. Med. Assn., 1910, liv, 1304; ibid., lv, 309; Wilder: Jour. Inf. Dis., 1911, ix, 9.

[3] Anderson and Goldberger: Bull. Hyg. Lab., U. S. P. H. S., 1912, No. 86.

louse transmission did not obtain a sufficiently definite rise in temperature to permit of a positive diagnosis; reliance was placed primarily on the appearance of malaise and on the immunity test. Nicolle in contrast to the other authors found that monkeys infected by the bites of lice showed two distinct febrile periods. The accompanying outline gives a summary of the results of these authors.

EXPERIMENTAL TRANSMISSION OF TYPHUS TO MONKEYS BY THE BODY LOUSE

	Feeding experiments			Injection of emulsions of lice		
	Positive	Negative	Doubtful	Positive	Negative	Doubtful
By Nicolle and His Collaborators						
No. of experiments	4 [a]	3 [b]	0	4	6 [c]	
Anderson and Goldberger [d]						
No. of experiments	1 [e]	2	1	0	4	1
Ricketts and Wilder						
No. of experiments	7 [f]	3	0	2	1	

(*a*) These animals are regarded as positive by the authors on account of their temperature reactions but three of the four might more critically be considered doubtful or negative.

(*b*) Two of these three negative animals were bitten by lice which had fed on typhus patients only four days previously.

(*c*) These animals were injected with lice which had their infecting feeding two to seven days previously.

(*d*) Anderson and Goldberger obtained positive results also with head lice.

(*e*) The temperature reaction in this animal was not very convincing.

(*f*) Typical temperature reactions were not obtained but typhus was diagnosed because these animals appeared ill.

Some evidence is also available in regard to the transmission by the louse in man. Two of Nicolle's laboratory attendants in Africa were accidentally bitten by lice that had fed on infected

monkeys. These attendants did not develop typhus fever. In another instance an attendant in a jail in Africa transferred lice from a typhus patient to a healthy individual. This individual developed typhus after the usual incubation period. While this patient was presumably not exposed to typhus in any other way the conditions were not under control and no definite conclusions are permissible.

While no direct experiments on man have been undertaken, some data were obtained by Sergent, Foley, and Vialatte [1] in the course of some work on relapsing fever. A normal man, who was bitten by lice that had fed upon a case of relapsing fever, developed as a consequence typhus fever. A second individual injected with lice that had fed on this case of relapsing fever and a third man injected with eggs of these lice also developed typhus fever. Apparently none of these individuals developed relapsing fever, although the lice contained large numbers of spirochaetes. These authors conclude that the case of relapsing fever must have been infected also with typhus fever and that the latter was transmitted by the bites and by the injection of the lice.

Although there is considerable confusion in the data of the experimental transmission of typhus to monkeys, still there is good reason to accept the idea of louse transmission of the disease both experimentally in animals and in man under natural conditions. Such circumstantial evidence as we were able to obtain in Serbia was in full accord with the theory of louse transmission. Certainly the vast majority of all patients had been bitten repeatedly by lice. However, with the approach of hot weather the incidence of typhus and of relapsing fever appeared to diminish more rapidly than the disappearance of lice.

It should be emphasized that the establishment of louse transmission does not militate against the possibility of the disease being transmitted by other methods also. Indeed the possibility of droplet infection in typhus must be considered

[1] Sergent, Foley, and Vialatte: Compt. rend. Acad. d. sc., 1914, clviii, 964.

seriously. A few cases of typhus developed in the Lady Paget Hospital among the staff under circumstances which permitted careful observation. Some of these cases seemed to be directly traceable to louse infestation; others could not readily be explained on this basis. This was especially true in the case of a nurse who protected herself carefully against insects in all of her hospital work. Toward the end of the epidemic, the ward under her charge had been free from active cases for about ten days when a patient extremely ill with typhus was admitted. It happened that this case had developed serious mouth, throat, and lung complications, necessitating frequent sponging and swabbing, the cleansing process often provoking more or less coughing. It is significant that both this patient and presumably the ward itself were free from lice, that the nurse also wore an effective louse-proof suit, that at no time had she any reason to suspect louse contamination, but that she did not wear the gauze masks providing for protection against droplet infection. No further typhus cases came under the care of this nurse; about two weeks later in Belgrade, while en route to England, in surroundings perfectly free from typhus, she developed a typical attack of the disease. While none of those instances occurring spontaneously under natural conditions can afford any exact proof, nevertheless they are sufficiently striking to merit consideration.

The members of the Commission working in the hospital with typhus cases adopted precautions both against insects and against droplet infection, although some authorities advise against the employment of precautions for droplet infection. The precautions taken against the louse were twofold in their nature, consisting in the destruction, as far as possible, of the lice and the wearing of the louse-proof uniforms. In the first place, the entire hospital was theoretically free from lice, all patients being carefully cleansed before admission. Practically, it was impossible to keep the wards absolutely and constantly free from lice though the living quarters of the staff were always free from such contamination. Accordingly the louse-proof suits were worn only in the wards and were then

left in a changing room and were never worn in the staff quarters. This regime necessitated the use of a fresh uniform at each visit to the wards. The uniforms for each day were collected and exposed overnight to chloroform vapor and were then ready for use the next morning. This procedure for destroying lice was suggested by Dr. C. T. Brues of Harvard University and it proved to be very simple and effective. In addition to the use of these uniforms, antiseptic baths were taken at the end of each day's work.

An ordinary surgeon's mask was used for protection against droplet infection. Essentially no other precautions were adopted.

Boston, Mass., December, 1915.

PART IV

REPORT OF BACTERIOLOGIST OF THE AMERICAN RED CROSS SANITARY COMMISSION TO SERBIA

By HANS ZINSSER

The bacteriological supplies were shipped on March 19, and the writer left with the main party of ten on the *Ducca d'Abruzzi*, on April 3. He arrived at Uskub (Skoplje) on the evening of May 1, where a general survey of the contents of the hospitals was made. After consultation with Dr. Strong it was decided that the bacteriological work should begin at Skoplje, since there seemed to be a greater concentration of typhus material here than in other places. Accordingly, about a week after arrival at Skoplje the writer, together with Doctors Shattuck and Sellards, moved out to the Sixth Reserve or Lady Paget Hospital, situated on the heights along the Vardar, about two kilometers outside of the town. There were said to be at that time a few more than 400 cases of typhus fever at the hospital. There was a very small room which the British unit were using as a laboratory, equipped only for the simplest clinical tests, available at the time, but such as it was, the full courtesies of everything at hand were extended by the British physicians. The writer wishes to lay stress at this place upon the generosity and uniform courtesy with which the officials of the Serbian government and the British hospital received and treated the American workers at Uskub throughout their stay.

Establishment of Laboratory

The first task, of course, was the establishment of a bacteriological laboratory in which suitably controlled work could be done, the writer conceiving it as his mission not only to work

on typhus, but to attempt the establishment of a laboratory to which the general bacteriological and sanitary work of the Commission could be referred. Although the supplies shipped from New York had not arrived, and did not arrive at Skoplje until May 17, the interval was spent in becoming familiar with typhus in its clinical aspects, the preparation of a laboratory space and autopsy room, and the performance of autopsies. By the courtesy of the Serbian government, a portion of the main artillery shed next to the Administration Building was placed at the disposal of the Commission for the establishment of a laboratory. A partition had been put up in this shed, but otherwise it consisted of a bare cement floor, with windows unsuitable for microscopic work, without running water, without electricity, and without gas. The labor of several Austrian prisoners and of a local carpenter were placed at the disposal of the bacteriologist, and the space was divided into a smaller autopsy room and a main laboratory room. Windows were broken through the walls, another door was broken through, cement sinks were put in, and a pipe was run from a well, in the yard, to the laboratory. A tin tank of about four cubic feet capacity was found and placed on the partition between the autopsy room and the laboratory, and from this, pipes were run to the sinks. When the supplies arrived it was found that the box containing thermometers, syringes, and the more expensive smaller apparatus — platinum wire, etc. — had been lost in transit. The electrical apparatus taken along, as well as that requiring gas, could not, of course, be used. Fortunately, a petroleum lamp incubator had been taken, and Primus kerosene stoves were bought. The British laboratory worker, Dr. Dalyell, permitted the transfer of all her available apparatus to this laboratory, joining forces with the American laboratory. Without this aid and coöperation the work of the Commission would have been very seriously hampered, because of the fact that so much of the apparatus brought was not suitable for the conditions encountered. Finally the apparatus was put in place and the laboratory was in suitable working condition by about the twenty-fifth of May.

During the period preceding this, the writer thought that although not all the criteria for properly controlled bacteriology could be fulfilled under the circumstances, it would be better to begin work with what was available. Fortunately, by the foresight of Doctors Shattuck and Sellards, some extra supplies had been taken with the party of ten, some of which duplicated the special bacteriological orders, and with these, together with what was borrowed from the British, work was begun. An Austrian prisoner, placed at the disposal of the bacteriologist, was trained as a laboratory assistant, was taught to make agar, broth, sterilize, etc. Autopsies were done on most of the cases of typhus that died during this time, and smear studies were made from the spleen and organs.

Bacteriological Examinations

Cultures also were made, from the spleen and heart's blood and other organs, but one or two of these only were of any great value, since most of the cases that died at this time died very late in the disease, after the temperature had been normal for anywhere from two to ten or twelve days, and secondary invaders, such as streptococci and Gram-negative bacilli, were often found in these cultures. Blood cultures were made at this time on many of the living patients, although few of the cases were in the early stage of the disease when they came under observation at the hospital. The large majority of the cases that came in were well along in the disease, having often been brought in from considerable distances under conditions that did not permit speed of transportation. In none of these early cultures was it possible to fulfill the criteria laid down by Plotz for the cultivation of his organism. Ascitic fluid was hard to obtain, since at this time almost all the patients in the hospitals were either typhus or relapsing fever, and small specimens of chest fluid only could be obtained. These were often not sterile, and in no case during this early period did we obtain an ascitic fluid of 1015 specific gravity or over, which could be used in the unheated and unfiltered condition as required for the Plotz method.

During this period, blood culture "5," taken with one of the specimens of chest fluid, which showed no growth in the controls, showed in a high tube in glucose agar a colony about two inches from the top, not gas-forming, with a white halo about it due to acid formation, which on fishing showed a short bacillus, slightly diphtheroid in form, morphologically corresponding roughly to the organism of Dr. Plotz. Comparing smears from an old culture of the Plotz bacillus with this organism, great similarity was seen, except that our organism appeared to be very slightly larger than the Plotz organism and a little more irregular in form. We were not successful in carrying this culture to the second generation, probably because we were at that time not in possession of suitable ascitic fluid. We wish to emphasize distinctly that we did not, at this time, consider our blood culture "5" of great scientific value because the ascitic fluid with which it had been taken had not been sufficiently controlled before use.

When our own supplies arrived it was found that all the ascitic fluid shipped from New York was either contaminated or probably because of aging and shaking had settled out, so that its specific gravity in no case exceeded 1012. However, by this time (the end of May) cases of ascites appeared at the hospital, and these were tapped. From two cases, ascitic fluids "X" and "Y" were obtained, fluids which we thought more nearly approximated the conditions set down by Plotz. With these fluids a number of blood cultures were taken, "X" having been well tested for sterility. In some blood cultures both fluids were used. From blood culture "5" to blood culture "35" no repetition of the diphtheroid anaërobic organism was obtained; a majority of these cultures were negative when the control tubes were negative, in two of them streptococci were obtained, and, in several others, large Gram-positive bacilli were present, which were taken to be evidences of contamination. It may be said that all blood cultures which showed any evidence of contamination were indiscriminately thrown out. It should also be stated that during this period hardly any of the cultures could be taken before what we would consider at

least the eighth or ninth day of the disease, and most cases were older than this. In blood cultures "35" and "38," one of which (38) had developed in the hospital, early blood cultures were obtained, most of the tubes being taken with ascitic fluid "X." In one tube of each of these a number of heavy colonies containing small Gram-positive diphtheroid bacilli were found, but these diphtheroid organisms showed great similarity to contaminating diphtheroids found in control tubes with one of the other ascitic fluids. These colonies, therefore, were not considered to have any significance. In blood culture "41," another early case which had developed in the hospital, the blood culture was taken on what we assumed to be the third or fourth day of the disease. In this case ascitic fluids "X" and "Y" were employed in different tubes. This blood culture was taken on June 12. By the twentieth two of the tubes taken with ascitic fluid "Y" were grossly contaminated. On one tube with "X" ascitic fluid which had shown no contaminations in controls, a suspicious colony appeared, which showed small Gram-positive bacilli, which were transplanted on ascitic agar slants in Buchner tubes and in ascitic glucose agar stabs in Buchner tubes. Two of the transplants grew. This culture, in the original appearance of the colonies, in the appearance of the transplants, their anaërobic growth requirements, and their morphology and staining properties corresponded to the Plotz organism.

We may briefly summarize the results of something over forty blood cultures on cases of unquestionable typhus by stating that only two of these showed organisms which corresponded to the Plotz bacillus. Cultures from the older cases showed occasional streptococci and Gram-negative bacilli, as did many of the cultures taken from recently dead bodies at autopsy, and these we regarded as secondary invaders. Indeed, we obtained the general impression that secondary bacterial invasion of the blood stream was not uncommon in typhus fever.

It did not seem to the writer that his own experience justified drawing definite conclusions about the Plotz bacillus. His opinion was against the aetiological significance of this organ-

ism because of the rarity with which it had been found, and because of the fact that the necessity of using unfiltered and unsterilized ascitic fluid in these cultures made it impossible to exclude absolutely that the organisms had originated in the ascitic fluid rather than in the case. While the difficulty under the circumstances of adhering accurately to the criteria set down by Plotz for the cultivation of his organism did not permit the writer to draw definitely negative conclusions concerning this organism, yet he felt that his work as a whole was more against it than in its favor.

The laboratory meanwhile had been, we consider, well organized, and it had been possible to extend its facilities to Dr. Castellani, who, with his personal assistant, used it during this period to make large quantities of cholera and typhoid vaccines for the use of the Commission for the Serbian army. Autopsies had been done on typhus cases and on other cases which interested the various physicians at the hospital whether or not typhus, and the laboratory was made as generally useful to the hospital as a whole as was possible at the time. During this time also it was used by Dr. Sellards in the pursuit of his special studies until his departure for Belgrade.

Guinea pig work was necessarily limited since three guinea pigs only survived, of the fifty taken from New York, probably owing to the rough weather and cold on the way over, which took pretty nearly a month, with many changes of weather and many transshipments en route. Five further guinea pigs were obtained at the end of May by the great courtesy of Dr. Kopanaris, sanitary chief of Greek Macedonia, in Salonika. Inoculations into these, intraperitoneally, of blood directly from the patient were made immediately after arrival at the hospital, and one of these after twelve days showed what we considered a typical rise in temperature. A transfer from this pig to another resulted in a temperature suggestive of typhus, though it did not exceed 104°C. at any time. Transfers from this one were also made, but showed no temperature reaction.

When the Kopanaris pigs arrived, all of them were injected from patients at various times, and in a number of them the peritoneal cavity was punctured by the Pfeiffer method, two, three, and six days after inoculation with the typhus blood, and cultures and smears made from the puncture fluid. In one of these pigs small Gram-positive bacilli were seen on the third day after inoculation with typhus blood. Smears of this pig were studied very carefully, both by the writer and by Dr. Castellani, and both believed that they were in a general way similar to the Plotz organism, but none of the other pigs showed such organisms, and cultures from the pigs with the materials used both aërobically anaërobically were entirely negative. Two of the pigs were injected rather a short time before leaving in the hope that the virus might be kept going for Dr. Hopkins on his arrival.

Vaccination

At about this time the question arose whether or not the Serbian troops should be vaccinated with the Plotz organism. The question was put to the bacteriologist by the director, Dr. Strong, and, as may be easily seen from the above report, the writer was not yet in a position at this time to either confirm or deny the aetiological importance of the Plotz organism. The isolated apparently positive findings in the blood cultures described above were not deemed by him sufficient basis for advising extensive vaccination which would subject the Serbian government to much administrative trouble, to expense, and difficulties of mobilization at a time of critical military necessities. Moreover, the epidemic was distinctly on the wane at this time, the decline being progressively more rapid as the weather turned warmer. The writer, therefore, distinctly advised the director that there was no information at his disposal at this time to justify a general vaccination of Serbian troops and population. This statement is made in order to make clear that in omitting a vaccination order at this time the director of the expedition asked the advice of the writer and obtained the above negative reply.

The writer started South on the twenty-ninth of June after turning over his material to Dr. Sellards and leaving the laboratory under the direction of Dr. Castellani. Dr. Sellards took charge of the typhus materials and the culture of the supposed Plotz organism isolated from the case above described, which he turned over to Dr. Hopkins who came over shortly after to continue the work.

PART V

SUPPLEMENTARY BACTERIOLOGICAL REPORT OF THE AMERICAN RED CROSS SANITARY COMMISSION TO SERBIA

By J. GARDNER HOPKINS

The writer left New York on the steamship *Thessalonica* on June 19 and arrived at Skoplje on July 19. Typhus had been for some time on the decrease, and by this time there were very few acute cases available for study. On arrival at Skoplje, however, it was found that a dozen cases from the civil jail at Cavadara had recently been brought to the Sixth Reserve (Lady Paget) Hospital, five of which were in the acute stage of the disease, and the writer proceeded at once to the hospital to study these cases. He found there a well-equipped bacteriological laboratory, which had been organized by Dr. Zinsser and his coworkers, which was then being used by Dr. Castellani of the American Commission for the preparation of typhoid, paratyphoid, and cholera vaccines for the Serbian army. There were two Austrian prisoners, assigned to laboratory duty, whom Dr. Zinsser had trained in the work. The use of the laboratory was put entirely at the disposal of the bacteriologist, and he was also given full charge of the typhus cases through the courtesy of Dr. Maitland, the chief physician of the Lady Paget Hospital. Cultures were made from one case with materials at hand in the laboratory, and as soon as agar, pleural fluid, and blood serum could be prepared, cultures were taken on other acute cases. Two days later an additional case in the acute stage of the disease was brought in from Cavadara.

Blood Culture Studies

Cultures were made by the method described by Plotz, the blood being taken from the arm vein with a sterilized syringe, and mixed with 2 per cent glucose agar, to which ascitic fluid or

human blood serum was added. The mixtures were made in deep tubes, and some of the tubes from each of the first eight cultures were placed in Buchner tubes before the agar had solidified. Considerable emphasis has been laid by Plotz on the specific gravity of the ascitic fluid used in the culture, and some difficulty was found in obtaining fluid which answered the requirement, that is, in which the specific gravity was over 1015. The only fluids available at the hospital were those obtained from cases of pleurisy with effusion, in which the specific gravity ranged from 1011 to 1018. In one culture a specimen of ascitic fluid was employed which had been kindly furnished by Dr. Plotz and had been found satisfactory in his work at Mount Sinai Hospital. In other cultures blood serum obtained by venesection in cases of nephritis was used, as it seemed that this must have all the advantages of a specimen of ascitic fluid with high protein content. Other specimens of ascitic fluid of lower specific gravity which had been brought from New York were also used.

The cases from which the cultures were made were all considered by the physicians who had studied the typhus epidemic in Serbia to be typical cases of typhus. They had high, continuous fever, ranging from 102° to 105° and profuse rash appearing, in some cases, on the palms of the hands. The cultures were all made during the febrile period, from the seventh to the eighteenth day of the disease, as nearly as could be ascertained from the history.

Twelve cultures in all were taken from the six cases available, and were observed for at least three weeks' incubation. The tubes before being discarded were emptied into sterile Petri dishes and the cylinder of agar cut into thin slices in order to detect any small colonies which might have escaped observation in the rather opaque medium. A number of tubes showed surface contaminations, due probably to the fact that the wards in the hospital were exceedingly drafty and it was impossible to avoid occasional contaminations from dust. In only one instance, however, was a deep growth obtained which in any way resembled the organism described by Dr. Plotz.

This one positive culture, No. 10, was obtained on the fifteenth day of the disease from a patient who died the following night. The temperature at the time of the blood culture was 102°. Two tubes from this culture showed each a single large colony in the depth of the medium, which appeared after ten days of incubation. The colonies were surrounded by a zone of precipitated albumen and showed morphologically small Gram-positive bacilli, strongly resembling those in the culture which had been furnished by Dr. Plotz. On subculture the organism proved to be an obligate anaërobe, until it had been preserved on artificial media for nearly two months, after which very faint growth in aërobic cultures was obtained. Like the Plotz organism it rapidly produces acid in glucose serum media as shown by the precipitation of the protein. It grows somewhat more heavily than the cultures of Dr. Plotz which the writer has seen, and produces deep yellow pigment, at times with a pinkish tinge. Inoculation of the culture in the third generation into a guinea pig was without result. Since this organism showed no pathogenicity, did not give the agglutination reaction described by Plotz and Olitsky, and resembled organisms described by Torrey as occurring as saprophytes in pathological lymph-nodes, it could not be regarded as significant.

Agglutination Studies

As the patient from whom the culture was obtained died before recovery of the bacillus, it was impossible to test the organism against his own serum. Macroscopic and microscopic agglutination tests were, however, carried out with the serum of convalescent typhus cases in the hospital which had had a normal temperature for a period of ten days to several weeks. Later, on going to Nish, a case was found which had had a normal temperature for only five days, and serum obtained through the courtesy of the Russian Red Cross physician in charge was also tested against the organism in question. None of the typhus sera gave definite agglutination in excess of that obtained in normal controls.

Autopsies

Autopsies were performed on three cases of typhus that died during the febrile period. Cultures made from the spleen were negative except for post-mortem contaminations.

Guinea Pig Inoculations

Two guinea pigs were inoculated from acute cases in the Lady Paget Hospital, and one from an emulsion of spleen of a typhus case obtained at autopsy, but no typical reactions were obtained.

Later Cases

As no further cases of typhus were available at the Sixth Reserve Hospital, attempts were made to locate cases suitable for study in other parts of the country. On a rumor that cases were developing in Galičnik, on the Albanian frontier, a trip was made to this place with a bacteriological outfit in the hope of obtaining specimens, but the rumor turned out to be false. Later two cases were located at Mladinowatz. These were mild cases, and were seen in conjunction with Dr. Sellards, Dr. Baehr, and Dr. Plotz. Dr. Baehr and Dr. Plotz made cultures from these cases, and Dr. Sellards and the bacteriologist inoculated a monkey and four guinea pigs, all of which failed to react. Other guinea pigs injected from these animals at a time when reaction might have been expected also failed to show any characteristic rise of temperature. Two cases of probable typhus were also visited at the Serbian military hospital at Ralja. Blood cultures taken from these cases were negative. Although they were considered typhus by the physician in charge, they were certainly not outspoken cases.

Results

Of six outspoken cases of typhus studied in the acute stage, all gave negative blood cultures except one. From this an organism resembling the Plotz bacillus was obtained, but, as it failed to agglutinate in serum of typhus patients and failed

to produce any typical reaction in a guinea pig, it was discarded. The results of these studies were not conclusive on account of the few cases available for study. However, the failure to isolate an organism corresponding to that described by Plotz, from the typical cases studied, has a certain value as negative evidence. While these experiments are too limited to be considered as disproving the reports of Plotz and his coworkers as to the aetiology of typhus, they failed to confirm these results, and the writer so reported to the chief of the commission, Dr. Strong.

As there seemed little likelihood of obtaining further suitable material for study, the writer left Serbia on the fifteenth of September.

In conclusion, acknowledgment should be made of the hospitality and courtesy extended by Lady Paget's British unit in charge of the Sixth Reserve Hospital and the invariable courtesy of the Serbian physicians and officials.

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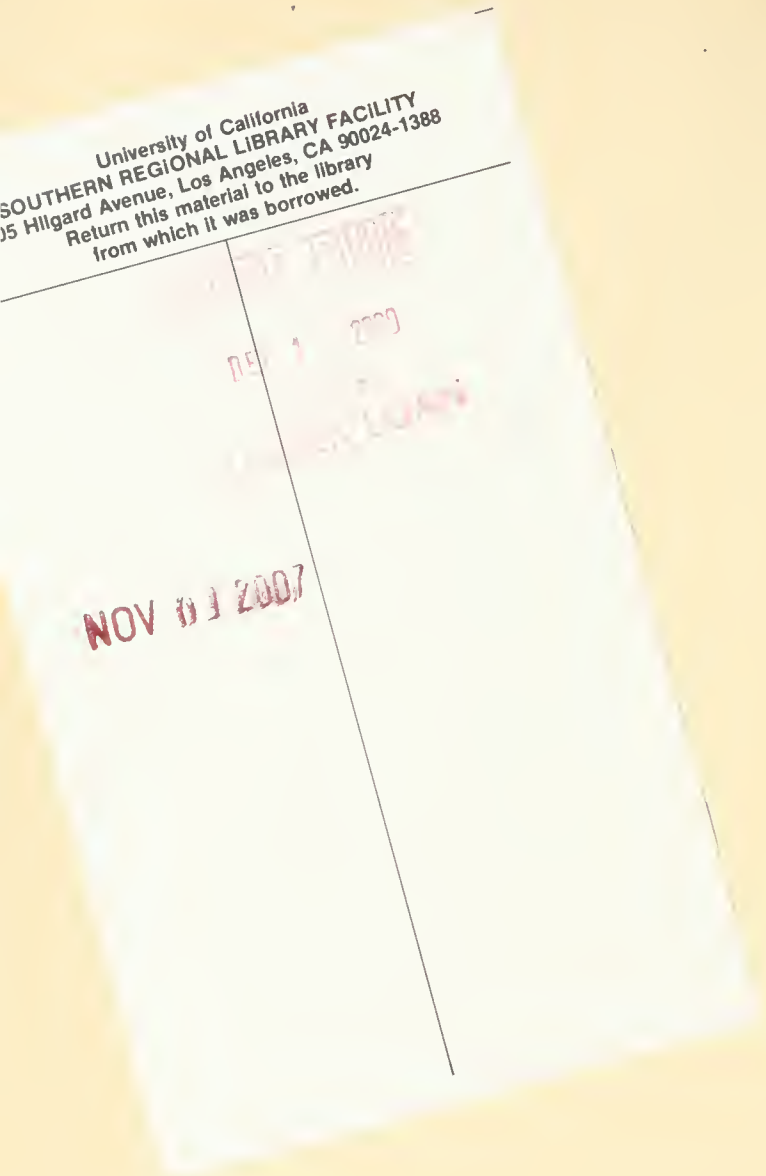

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